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ON

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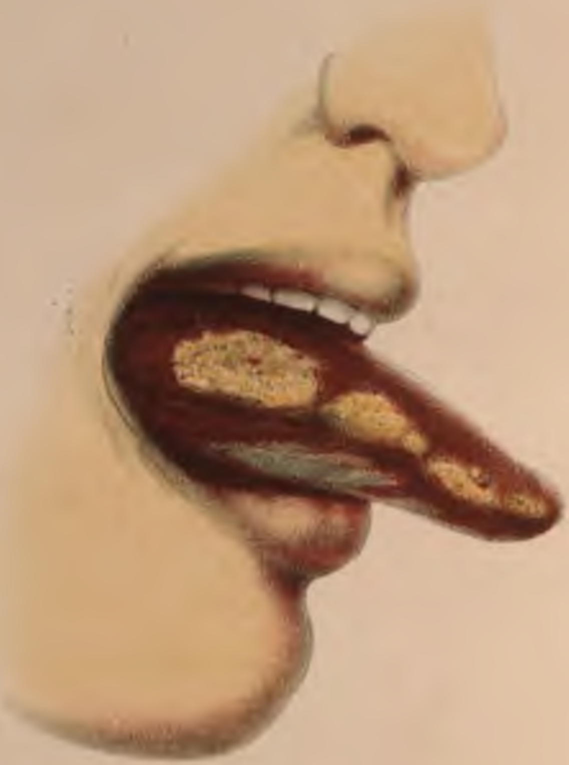

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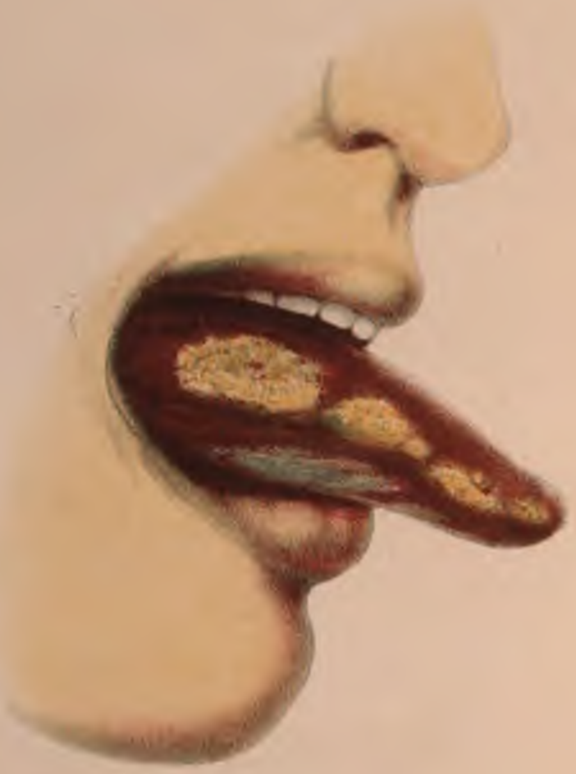

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ON THE BILE

JAUNDICE

AND

BILIOUS DISEASES

BY

J. WICKHAM LEGG

FELLOW OF THE ROYAL COLLEGE OF PHYSICIANS OF LONDON
ASSISTANT PHYSICIAN TO SAINT BARTHOLOMEW'S HOSPITAL AND LECTURER ON PATHOLOGICAL ANATOMY IN THE MEDICAL SCHOOL

> *La bile est un liquide dont l'étude intéresse au plus haut point le physiologiste et le médecin. Les difficultés dont est entouré son histoire physiologique font qu'elle est encore fort obscure.*
>
> CLAUDE BERNARD.

NEW YORK
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M. DCCC. LXXX.

has been made in the knowledge of the changes which they undergo in disease. Some observations made at St. Bartholomew's Hospital in the year 1873, on the amount of glycogen in the liver in jaundice, are among the first attempts to tread this path of experiment.

The following pages are devoted to that office of the liver which, for two hundred years, was the only one allowed by physiologists; that is, the secretion of bile. The early chapters treat of the chemistry and physiology of this humour. The first of these may be thought to be in a tolerably satisfactory state, since so much light was thrown upon the chemistry of the bile acids by the labours of Adolf Strecker thirty years ago. The physiology of the bile is still surrounded by a darkness almost Egyptian; and it may surprise many to find how little knowledge there is of a humour which has been carefully studied for over two thousand years, and which already filled a great place in the physiology of the *Timæus.* Much of this obscurity is doubtless due to the place which physiology holds among the sciences; little progress can be made till the others beneath have well nigh reached perfection; and still more to the point at which the bile is discharged, into the upper part of the intestine, where it cannot conveniently be collected and measured, as may readily be done with other secretions, such as the urine. A bar, not to be overcome, seems to be thus placed by nature herself in the way of much increase of knowledge.

In several chapters, the phænomena caused by an obstruction to the discharge of the bile into the intestine have been dealt with; and in those which follow, an account has been given of certain species of jaundice, where an obstruction to the flow of bile cannot at once and without trouble be discovered after death. And to those species of jaundice, the cause of which is obscure, I have confined myself; though, nevertheless, I have not fallen into the un-English virtue of consistency; for, as part of the chapter on *icterus infantum*, I have dealt with the appearances which follow congenital constriction of the gall ducts, which may by some be considered only a variety of the foregoing *icterus*. In a work, too, which deals with disorders of the bile, some account of gall-stones might be looked for; but the space required for anything like a full discussion of the phænomena caused by these bodies would be very great, and I have already gone beyond the bounds which were set when the printing of this book was begun. Sometimes, too, I have had to travel twice over the same ground in dealing with the physiology of the bile and the doctrine of jaundice; and there thus arises the appearance of repetition, very needful, however, to the right understanding of the matter in hand.

In the last chapter I have specially considered the meaning of "bilious diseases"; and I have proposed that the word "bilious" should no longer be used as an adjective to diseases. I am led to this proposal by the great confusion which exists as to the definition of the word; nearly every country, and I might say, nearly every author, having a different sense for it. In this work, "bilious," when used with the word headache, attack, or the like, always connotes a gastric catarrh.

I am glad of this opportunity to thank Professor Chauveau and the French Government for the hospitality shown to a foreigner in providing the means for some experiments which were made at Lyons nearly two years ago, and of which I have spoken in the fourteenth Chapter of this work. All the appliances of one of the best furnished laboratories in Europe were set before me; a staff of able assistants was told off to give me whatever aid was needful; and the cost of the whole series of experiments was borne by the French Government. It would be indeed ungrateful not to acknowledge, even in this feeble way, the welcome which I received. It may strike others, besides myself, that much light would have been thrown upon many other points in this work by well-devised experiments. But in England, for some years past, all experiments on animals have been practically forbidden. We pay for our freedom in some matters by being at the mercy of every truculent agitation in others; and a senseless outcry, by putting on the sacred garb of religion and morality, from the highest authorities in which it receives no countenance, but rather condemnation, has prospered in its designs for a time. In the plan of the book I have therefore followed the method of Albert the Great, rather than the higher path shown us by Francis Bacon, and our own great predecessor at St. Bartholomew's, William Harvey. For whatever imperfections there may be in the method followed, the reader must blame those Manichæan teachings, which, harmful as they are, are almost as old as the human race itself, and the germs of which seem to exist everywhere, ready to burst into a fresh life, even amongst those who claim to be most orthodox and sincere in their morals and belief.

London, Dec. 20, 1879.

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ERRATA.

p. 72, Heinrich Bayer's paper on human cholalic acid appears in the September number of Hoppe-Seyler's *Zeitschrift f. phys. Chemie*, 1879.

p. 148, second line from top, for *chloidic* read *choloidic.*

p. 485, third line from top, for *blood from the urine* read *blood from the arm.*

p. 491, third line from top, for Moraud read Morand.

CHAPTER I.

CHEMISTRY OF THE BILE.

THE bile of vertebrates is made up chiefly of three groups of bodies: the bile acids in combination with soda; the bile pigments; and fats, especially cholestearin. Of these, the bile acids are by far the most noteworthy, as they are found in greatest amount, and are the most important in their physiological action and relations.

It cannot be looked for that much information should have been gained as to the chemical composition of the bile before the time of Lavoisier. But it needed no chemist to say that the bile held a pigment: and it was well known that it possessed the power of cleaning stuffs like a soap.[*] Robert Ramsay appears to have been the first to note the resin in the bile which was afterwards to be known as the bile acids,[†] but it is to the very beginning of this century that we must look for the first satisfactory attempts at an analysis of the bile.

Thenard, by throwing down the bile with the acetate of lead, an agent which has proved so useful in the manipulation of this humour, obtained a body which he named picromel,[*] from its taste. This appears to have been a collection of the impure bile acids. He also separated a resin or fat, to which he attributed in chief the colour and taste of the bile. He opposed the ancient belief that the bile was a kind of soap. He noted the amount of soda salts, the presence of traces of iron, and that the solids were about $\frac{1}{8}$ to $\frac{1}{9}$.[†]

---

[*] Cadet, *Mémoires de l'Académie royale des Sciences*, année 1767, Paris 1770, p. 483. "Je puis donc enfin conclure que la bile est un véritable savon composé d'une graisse animale et de la base alkaline du sel marin, et du sel marin lui-même, d'un sel essentiel de la nature du sucre de lait et d'une terre calcaire qui participe un peu du fer." For history of earlier opinions, see Haller, *Elem. phys.* Lugd. Bat. 1764, t. vi. p. 542. Lib. xxiii. § iii. For history up to his own time, see Platner, *Ueber die Natur u. den Nutzen der Galle*, Heidelberg, 1845.

[†] Roberti Ramsay, *Diss. Med. inaug. de bile*, Edinb. 1757, in Sandifort's *Thesaurus Dissertationum*, Roterodami, 1769, vol. ii. p. 567. "Bilis materiis constare videtur tribus diversis, parte scilicet aquosa; parte resinosa, spiritu vini, non aqua solubili; parte denique viscida putrescente, neque aqua, neque spiritu vini solubili".

Berzelius followed hard upon Thenard with his investigations on the bile. He thought it probable that the picromel and resin of Thenard were but one body. Berzelius named this biliary material ;[‡] it was, in his opinion, free from nitrogen but akin to albumen.

Tiedemann and Gmelin report a large number of analyses of the bile in their work on the digestion of animals.[§] They claim to have noted the presence of cholestearin in the bile in the year 1823, before they were acquainted with the work of Chevreul, and also to have discovered in the winter of 1823-24 the action of nitric acid on the colouring matter of the bile.[‖] They also affirmed the presence in the bile of margarates, oleates, acetates, cholates, bicarbonates, phosphates, and sulphates of soda, and a body which they called asparagin but which it is possible was taurin. A few years later, Fromherz and Gugert[¶] came to results very nearly allied to those of Tiedemann and Gmelin. Ten years later Demarçay succeeded in separating three animal charcoal. This black mass is then put into a wide-mouthed bottle, shaken up with ordinary spirit, and allowed to stand for several days. The spirit is then filtered off from the black powder, and the filtrate evaporated to dryness. The dry residue is then dissolved in absolute alcohol and poured into a great excess of æther in a large stoppered bottle. If good crystals be looked for, it is well not to be too sparing with the æther and alcohol. After a few days or even longer, the milky fluid becomes clear, and crystals are deposited at the bottom. I have found this process more serviceable for the manufacture of large quantities of crystallised bile than either the process of Hoppe-Seyler or Kühne. Kühne, for example, evaporates the bile to one-fourth of its volume, then rubs up with animal charcoal, dries the mass at 100° C. then puts the whole, warm, into a large bottle, and exhausts with absolute alcohol. After some days, he filters, and throws down with æther. This is a wasteful method, as so much of the bile acids is retained in the animal charcoal. On the other hand, Hoppe-Seyler does not proceed to decolorise the bile until after the dried bile have been extracted with alcohol. He then evaporates the filtrate to dryness, and dissolves in a small quantity of absolute alcohol, precipitating by excess of æther.* Both these methods succeed on the small scale, but for the preparation of large quantities I prefer the plan mentioned first.

---

[*] Apparently compounded of πικρός, bitter, and μέλι, honey.

[†] Thenard, *Mémoires de Physique et de Chimie de la Société d'Arcueil*, 1807, t. j. p. 23. Lu à l'Institut le 2. floréal, an 13.

[‡] Berzelius, Schweigger's *Journal f. Chemie und Physik*, 1814, Bd. x. p. 488.

[§] Tiedemann and Gmelin, *Recherches exp. phys. et chimiques sur la digestion*, Jourdan's trans. Paris, 1826, Ière partie, p. 42.

[‖] Preface, p. xv. See Chevreul, *Journal de phys. exp. et path.* 1824, t. iv. p. 257. He certainly found cholestearin in the bile.

[¶] Fromherz and Gugert, Schweigger's *Journal f. Chem. u. Phys.* 1827, Bd. l. p. 68.

These colourless crystals are composed in the ox of the soda salts of the two acids; they are exceedingly deliquescent, and therefore very soluble in water. They have a peculiar bitter, sweet taste. They are soluble in alcohol, insoluble in æther.

Frerichs and Städeler found that, if the pure soda salts of the bile acids were acted on by strong sulphuric acid, there was formed at first a colourless mucilaginous mass which dissolved by degrees in the cold into a saffron yellow fluid, with heat into a bright red or brown-red fluid.[*] These authors thought this observation of much importance, showing the change of bile acid into bile pigment.

---

* Hoppe-Seyler, *Handbuch d. phys. und path. chemischen Analyse*, Berlin, 1865, p. 149.

It is to the presence of this 'crystallised bile' in the bile that this secretion gives the reaction named after Pettenkofer.[†] If to a watery solution of the bile acids strong sulphuric acid be added, the bile acids are first thrown down, and then re-dissolved by adding more sulphuric acid. If now a drop of syrup (cane sugar)[‡] be added to the warm solution, the temperature of which must not be allowed to rise above 70° C. a fine purple colour is developed; compared by Pettenkofer himself to a solution of permanganate of potash. The development of this colour constitutes Pettenkofer's test. The reaction is given by glycocholic acid, taurocholic acids, and many of their derivatives.

Neukomm found that a watery solution of the bile acids, ·4 *per cent.* in strength, gave a fine reaction: with ·1 *per cent.* the colour was purple red with a trace of violet: with ·04 *per cent.* only a weak wine red colour; and with ·01 *per cent.* only a yellow fluid which did not become red on standing. Neukomm thinks that the reaction becomes much more delicate if done in a porcelain dish in the following manner: a drop of the fluid to be tested is let fall into a Berlin dish with another drop of dilute sulphuric acid, one to four, and just a trace of solution of cane sugar added to the whole, and then it is rolled about over the flame of a spirit lamp. The heat used for the evaporation must be small. As the fluid evaporates, a fine red purple is developed. Neukomm says that in this way he has detected ·006 of a milligramme.[*]

---

[*] Frerichs and Städeler, *Arch. f. Anat. Phys. u.s.w.* 1856, p. 55.

[†] Pettenkofer, *Annalen d. Chemie u. Pharm.* 1844, Bd. lii. p. 90.

[‡] Jurasz (*Centralblatt f. d. med. Wiss.* 1875, p. 515) finds that the reaction also appears with grape and fruit sugar, most rapidly of all with this last; slowly with grape sugar. He thinks the ordinary reaction due to the splitting up of the cane sugar by the sulphuric acid into grape and fruit sugar.

Other modifications of Pettenkofer's test have been introduced, notably by Bogomoloff and Strassburg. Bogomoloff recommends that the bile acids be dissolved in alcohol, or that the watery solution have a great excess of alcohol added, and then evaporated over a water-bath in a porcelain dish, moving the dish gently about so that the bile acids may form a tolerably even coating over the dish. A drop, or two, of sulphuric acid is now let fall by means of a glass rod upon the dried bile acids, and in the same place a drop or two of spirit. A number of colours appear. In the centre, the colour is yellow, then around, first orange, then red, rose red, violet, indigo violet, indigo blue; lastly the whole spot becomes blue. By this method Bogomoloff says he has detected 3 milligrammes of bile acid in 15 C.C.[†]

Strassburg recommends another way, chiefly for the testing of urine. A little cane sugar is added to the fluid, and a piece of filtering paper is dipped into the mixture. The filtering paper is then dried, and on it is let fall a drop of strong sulphuric acid by means of glass rod; in a quarter of a minute a violet colour appears around the drop of acid.[‡] I cannot say that I have found this a trustworthy modification. A purplish colour may be seen in urine from many persons not known to be seriously disordered. Strassburg says he has detected ·00003 grm. of bile acid by this method.

---

[*] Neukomm, *Annalen d. Chemie und Pharmacie*, 1860, Bd. cxvi. p. 30.

[†] Bogomoloff, *Centralblatt f. d. med. Wiss.* 1869, p. 486.

[‡] Strassburg, *Arch. f. d. ges. Phys.* 1871, Bd. iv. p. 461.

A red or purple colour is given by many other bodies besides the bile acids. Pettenkofer himself noted that the reaction appeared with a solution of albumen, but not of mucus:[*] an observation which was confirmed by Max Sigm. Schultze, who found that muscular tissue, voluntary or involuntary, the crystalline lens, the nerve fibres, and ganglia, showed a red colour with sulphuric acid and sugar. The colour did not appear with tendons or connective tissue, so that the tissues rich in albumen gave the reaction, but not those rich in gelatin.[†] Beneke has noted the same appearance with chemically pure oleic acid, and with pure æther, and also under certain concentrations with cholestearin.[‡] Schneider, too, finds that morphia and cadeia give the same reaction, but not narcotin, nor narcein, quinine, strychnia, brucia, atropia, colchicin, emetia, or picrotoxin.[§] The reaction is said also to appear with amylic alcohol.

Koschlakoff and Bogomoloff, noting this false Pettenkofer's reaction with albumen and other bodies, say that the spectrum affords a sure means of diagnosis. The fluid of Pettenkofer's reaction is so deeply coloured that it must be diluted before light can pass through. This dilution is best done with acetic acid, as water throws down a violet precipitate. This fluid in the spectroscope shows with moderate concentration four absorption bands; the largest and most intensely marked, shows itself in E and a little to the left. The other in F. The third between D and E, nearer to

---

[*] Pettenkofer, *loc. cit.*

[†] Max. Sigm. Schultze, *Annalen d. Chemie u. Pharmacie*, 1849, Bd. lxxi. p. 273. Like observations have been made on the tissues of invertebrate animals by Friedrich Will (*Arch. f. Anat. Phys. u.s.w.* 1848, p. 502), and Voit (*Zeitschrift f. wiss. Zoologie*, 1860, Bd. x. p. 470.)

[‡] Beneke, *Studien ueber das Vorkommen, die Verbreitung und die Function von Gallenbestandtheilen, u.s.w.* Giessen, 1862, pp. 35 *et seq.*

[§] Schneider, *Annalen der Physik und Chemie*, 1872, Bd. cxlvii. p. 128.

D. The fourth near D. If the fluid be more dilute, the bands in E are well seen, between D and E much less marked, and in D and F very weak. With high concentration, the absorption bands in E and between D and E unite in one plainly marked band. In F there is a well-marked band. In D the bands are always well marked.

These observers also remark that the fluid of Pettenkofer's reaction shows a fluorescence, if well diluted with dilute acetic acid; it is green by reflected light; cherry red by transmitted light.* This observation has been repeated by Schenk; and he also finds absorption bands in the fluid of Pettenkofer's test, but they are somewhat different in place and number from those noted by Koschlakoff and Bogomoloff. If the solution be dilute there is seen at F an absorption band which fills about half the space between E and F; there is another band at the line E between D and E, and it fills half of this space. But if the solution be concentrated there is only seen one band between D and E.†

Dalton also found absorption bands in the alcoholic solution of Pettenkofer's reaction; two wide and dark bands, one at E, from D 50 E to E 25 F; the other at F, from E 60 F to F 15 G, the spectrum ending about G. A band at D was also frequently seen.

The solution in alcohol of the bile acids shows a spectrum in which the bands at E and F are visible and often also the band at D. It makes a great difference if alcohol or water be used as a solvent: the watery solution gives only one band at E. Beyond the bands the spectrum is dim.

---

* Koschlakoff and Bogomoloff, *Centralblatt f. d. med. Wiss.* 1868, p. 529.

† Schenk, *Anatomisch-physiologische Untersuchungen*, Wien, 1872, p. 47. I have not been able to find the observations of Waterman, as quoted by Schenk. On the contrary, Waterman says (*New York Medical Record*, 1871-2, Vol. vi. p. 436.) that normal bile is nearly devoid of the power of affecting the spectrum

There is no difference between the spectra of glycocholate or taurocholate of soda.

Dalton thinks that the characters of the spectrum of the fluid of Pettenkofer's reaction may be used to distinguish it from the red fluids obtained by a like reaction on morphia, albumen, and the like. He finds that the opium alkaloids give a band at E, but it is somewhat indistinct and disappears on dilution. Albumen gives a single band in the space between E and F, the edges are not well defined and the spectrum beyond is dim.* Bogomoloff finds that the spectrum of oil treated with Pettenkofer's method gives two bands: one, more intense than the other, between D and E, nearer to D: the other on the left of D.†

Glycocholic acid. For the knowledge of this acid we are indebted to Strecker, and according to his advice it is prepared by dissolving the crystallised bile from ox-bile in water and then throwing down the pure acid with dilute sulphuric acid. The addition of acid must be stopped as soon as a slight precipitate be formed. After a few hours the fluid is found full of stellate needles, which should be collected on a filter, washed with water, and pressed.

It is not needful, however, to use crystallised bile in the first instance; the acid may be thrown down from bile purified according to Theyer and Schlosser's method,‡ and the precipitate thrown into æther forms a heap of stellate crystals.§

Another way is to precipitate a solution of crystallised bile with neutral acetate of lead. After complete precipitation with this salt, a second precipitation may be made with basic acetate of lead to throw down taurocholate of lead. The precipitates are the lead salts of the two bile acids, glycocholic and taurocholic acid. The precipitates must be dissolved in hot alcohol, sulphuretted hydrogen passed through, and then water added to the concentrated alcoholic solution, which throws down the glycocholic acid.

---

* Dalton, *New York Medical Journal*, 1874, Vol. xix. p. 589.

† Bogomoloff, *Centralblatt f. d. med. Wiss.* 1869, p. 484.

‡ Theyer and Schlosser, *Annalen d. Chemie und Pharmacie*, 1843, Bd. xlviii. p. 77.

§ Adolph Strecker, *ibid.* 1848, Bd. lxv. p. 9.

Gorup-Besanez evaporates ox-gall almost to dryness in a water bath, and then extracts with alcohol of 90. *per cent.* The alcohol is distilled or driven off from the filtered solution, the residue is diluted with water and milk of lime is added, to throw down the pigment which combines with the lime. The somewhat yellow coloured filtrate is now first neutralised with sulphuric acid, and then just enough added to throw down the glycocholic acid, but all excess should be avoided. In a few hours the whole becomes a mass of crystals which must be filtered, washed, and pressed.*

A quicker way of preparing pure glycocholic acid is recommended by Hüfner. Fresh ox bile is put into a narrow cylindrical glass and æther poured on to the surface of the bile; then a strong mineral acid is added to the bile so as to throw down the bile acids. First a milky precipitate is formed which later on becomes crystalline, sometimes so rapidly that the whole mass becomes solid; the æther turns of a yellow or brown colour, but after standing some time becomes purple or violet. The mass of crystals must be separated from the æther and shaken up forcibly in a stoppered vessel, then put into a filter and washed on the filter with cold water until the filtrate cease to be of a green colour. This filtrate contains the taurocholic acid which is readily soluble in water. The glycocholic acid is not soluble in cold, but readily in hot, water: to purify the mass on the filter it must be dissolved in boiling water, rapidly filtered, and when cold the acid crystallises out in purity.*

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* Gorup-Besanez, *Annalen der Chemie und Pharm.* 1871, Bd. clvii. p. 286.

Our knowledge of the composition of glycocholic acid is entirely due to the labours of Strecker. He found that if glycocholic acid be boiled for many hours, about 24, with caustic baryta, that the glycocholic acid is completely decomposed into two bodies: cholalic acid and glycocoll :†

$$\overset{\text{Cholalic acid.}}{C^{24}H^{40}O^{5}} + \overset{\text{Glycocoll.}}{C^{2}NH^{5}O^{2}} - H^{2}O = \overset{\text{Glycocholic acid.}}{C^{26}H^{43}NO^{6}}$$

or in the old notation:

$$\overset{\text{Cholalic acid.}}{C^{48}H^{40}O^{10}} + \overset{\text{Glycocoll.}}{C^{4}NH^{5}O^{4}} - 2HO = \overset{\text{Glycocholic acid.}}{C^{52}H^{43}NO^{12}}$$

A like decomposition takes place if glycocholic acid be boiled with acids, especially hydrochloric acid: a precipitate is thrown down consisting of hydrochlorate of glycocoll, (glycin or glycocine). If this body be dissolved in water, and heated with oxyde of lead, the chloride of lead separated, and the superabundant lead removed with sulphuretted hydrogen, the filtrate may be evaporated for crystallisation. Glycocoll is a crystalline body; it forms large rhombohedra which are easily soluble in water, very little in hot alcohol, insoluble in cold alcohol and in æther. It is not needful to go deeply into the chemistry of this body in this work; but it is well to say that it is an amide uniting with both acids and bases: according to its composition it would be amido-acetic acid. It has been synthetically made by Perkin and Duppa from mono-brom-acetic acid,‡ and by Cahours§ from mono-chlor-acetic acid:

$$C^{2}H^{3}ClO^{2} + 2NH^{3} = \overset{\text{Glycocoll.}}{C^{2}H^{2}\,(NH^{2})\,O\,(OH)} + NH^{4}Cl$$

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* Hüfner, *Journal f. prakt. Chemie*, 1874, Bd. cxviii. p. 267.

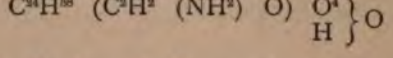
† Adolph Strecker, *Annalen d. Chemie und Pharmacie*, 1848, Bd. lxvii. pp. 2 *et seq.*

‡ Perkin and Duppa, *Phil. Mag.* 1857, Vol. xiv. p. 217.

§ Cahours, *Comptes rendus*, 1858, t. xlvi. p. 1044.

It may be prepared from gluten, and even in small amount from albuminous bodies. It is important to the physiological chemist because it enters into the composition of hippuric acid as well as of the bile acids. Hippuric acid is benzoic acid *plus* glycocoll. Hoppe-Seyler recommends glycocoll to be prepared by boiling hydrochloric acid with hippuric acid.* It has no influence on polarised light.

Glycocholic acid has not yet been made directly from a combination of cholalic acid and glycocoll. Glycocholic acid may be looked upon as a chol-amide acetic acid:



$$C^{24}H^{38}\ (C^{2}H^{2}\ (NH^{2})\ O)\ \left.\begin{matrix}O^{4}\\ H\end{matrix}\right\}O$$

The crystals of glycocholic acid are fine white needles, which even when looked at with a microscope magnifying 300 times, scarcely show a diameter.

Glycocholic acid is but slightly soluble in water; 1000 parts of cold water dissolve 3·3 of the acid; and the same parts of boiling water 8·3. The solution is sweet and somewhat bitter to the taste; it reddens litmus and shows no reaction with acids, acetate of lead, corrosive sublimate, or nitrate of silver; sub-acetate of lead causes a slight precipitate.

The acid is very soluble in alcohol; and if it be heated in a water bath becomes a syrupy, later on, a resinous mass, from which crystals cannot again be obtained.

In æther, glycocholic acid is but slightly soluble; but much æther must be added to a concentrated alcoholic solution before it be even partly thrown down.

Concentrated sulphuric, hydrochloric, and acetic acids dissolve glycocholic acid. Alkalies readily dissolve it. It expels the carbonic acid from the alkaline carbonates.

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* Hoppe-Seyler, *Handb. d. phys. und path. chem. Analyse*, Berlin, 1865, p. 124.

The combination of glycocholic acid with soda is that which is the most important, inasmuch as this is the salt which is found in the bile. It crystallises in white needles, just like crystallised bile. It is very soluble in water, less so in absolute alcohol. 1000 parts of alcohol dissolve at 15° C. 39 parts of glycocholate of soda.

There are also glycocholates of potash, ammonia, and baryta, all soluble in water.

De l'Arbre finds that the bile acids unite and form crystals with alkaloids, such as strychnine, brucine, morphia,* &c.

Hoppe-Seyler has found that the bile acids and their derivatives have a marked influence on polarised light. Glycocholic acid has a dextro-rotatory power for red light of $+27^\circ \cdot 22$: for yellow light $+29^\circ \cdot 93$; and it is inferred for sun light $+36^\circ \cdot 15$. The rotatory action is the same whether the acid be in combination with a base or not.†

Taurocholic Acid.—Strecker showed that the precipitate thrown down by sub-acetate of lead, after the precipitate thrown down by acetate of lead had been separated, contained an acid different from glycocholic, inasmuch as sulphur, as well as nitrogen, entered into its composition. He was, however, unable to separate the glycocholate of lead from the taurocholate; he therefore subjected the lead precipitate to the same process, boiling with baryta, that was so fruitful in the decomposition of glycocholic acid. A like decomposition did indeed set in; with cholalic acid, two bodies, taurin and glycocoll, were formed, instead of one, glycocoll. These two were readily separated by means of alcohol containing hydrochloric acid, in which glycocoll is readily soluble, while taurin is but very slightly taken up by it.* Taurocholic acid is therefore a compound of taurin and cholalic acid:

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* De l'Arbre, *Chem. Centralblatt*, 1872, p. 231. See also Malinin, *Centralblatt f. d. med. Wiss.* 1868, p. 370.

† Hoppe-Seyler, *Arch. f. path. Anat.* 1858, Bd. xv. p. 130. More elaborate observations by Hoppe-Seyler on this same subject will be found in the *Journal f. prakt. Chemie*, 1863, Bd. lxxxix. p. 257.

$$\begin{array}{ccccccc} \text{Cholalic Acid.} & & \text{Taurin.} & & \text{Water.} & & \text{Taurocholic Acid.} \\ C^{24}H^{40}O^{5} & + & C^{2}H^{7}NO^{3}S & - & H^{2}O & = & C^{26}H^{45}NO^{7}S. \end{array}$$

or in the old notation:

$$C^{48}H^{40}O^{10} + C^{4}H^{7}NO^{6}S^{2} + 2\,HO = C^{52}H^{45}NO^{14}S^{2}$$

Of taurin it will be enough to say that its formula was first accurately given by Redtenbacher,† and a rational formula by Kolbe.‡ It is amido-isæthionic (æthyl sulphuric) acid. It may be formed synthetically by heating the ammoniacal salt of isæthionic acid to 210° C.§ or else by the action of ammonia upon the chloræthyl sulphate of silver.

Taurin is a crystalline body, forming colourless prisms, quadrate, or oftener hexagonal, with four-sided pyramids at each end. Its solution is neutral and it unites with neither acids nor bases. This body is one of the richest in sulphur of those found in the œconomy. It has no action on polarised light.‖

Taurocholic acid may be obtained by decomposing its lead salt with sulphuretted hydrogen, filtering, and evaporating at a low temperature. It has not yet been seen in crystals;¶ it is, reversing the property of glycocholic acid, readily soluble in water. The solution is acid and soon decomposes, even on boiling. By boiling with acids or alkalies it is decomposed into taurin and cholalic acid.

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* Strecker, *Annalen d. Chemie u. Pharmacie*, 1848, Bd. lxvii. p. 31.

† Redtenbacher, *ibid.* 1846, Bd. lvii. p. 170.

‡ Kolbe, *ibid.* 1859, Bd. cxii. p. 241, and 1862, Bd. cxxii. p. 33.

§ Strecker, *ibid.* 1854, Bd. xci. p. 101.

‖ Hoppe-Seyler, *Arch. f. path. Anat.* 1858, Bd. xv. p. 132.

¶ J. Parke, Hoppe-Seyler's *Med. chem. Untersuchungen*, Berlin, 1866, p. 160.

Strecker describes the alkaline salts of taurocholic acid as very soluble in water and spirit, but insoluble in æther. They have no action on litmus paper. Exposed to moist air, they increase considerably in weight but do not deliquesce. When heated upon platinum foil, the salt first melts, then throws off bubbles, and burns, leaving behind it an ash. The watery solution tastes sweet with a bitter after-taste. The acid is not thrown down by acids, even by concentrated sulphuric acid. If boiled with acids, oily drops of choloidic acid are thrown down, and the fluid retains taurin in solution. By adding concentrated solution of potash to a watery solution of an alkaline taurocholate, the potash takes over completely the taurocholate to itself. In the same way the taurocholate drives out the carbonic acid of an alkaline carbonate; but has no influence on a sulphate or chloride. Carbonic acid does not unite with the alkali of any alkaline taurocholate in alcoholic solution. With lime, baryta, and magnesia salts there is no precipitate, nor even with ammonia. With neutral acetate of lead there is no precipitate, but white flakes are thrown down by the sub-acetate. These are dissolved by heat, and again thrown down by cooling, and are also soluble in a great excess of sub-acetate of lead. After complete precipitation with sub-acetate of lead, there appears a fresh precipitate with ammonia.

The watery and alcoholic solutions of taurocholates may be evaporated in a water bath without undergoing change; nor are they, if pure, decomposed by long keeping. The solution of the free acid cannot be evaporated to dryness without decomposition.

In watery solutions of alkaline taurocholates there is no precipitate with acetate of copper, but a little ammonia throws down bluish white flakes soluble in excess: nitrate of silver gives no precipitate, even with ammonia, and on boiling, a part of the silver is reduced. Perchloride of iron at first gives a precipitate soluble in excess. Perchloride of mercury gives no precipitate, but the nitrate of mercury and chloride of zinc throw down white flakes. Taurocholates give Pettenkofer's reaction.[*]

Hoppe-Seyler has found that the dextro-rotatory power of taurocholic acid for red light is $+ 24^{\circ}\cdot 92$; for yellow $+ 25^{\circ}\cdot 28$.[†]

The bile acids are not the same throughout the vertebrate sub-kingdom. The bile of the lower animals has been investigated by several chemists, chiefly by Strecker. It would seem probable that the nitrogenous bases of the bile acids are always the same, glycocoll and taurin, while the acid with which they are combined is the body which varies.

Strecker finds the bile acid of dogs to be entirely taurocholic without a trace of glycocholic:[‡] but Dr. George Scott found a glycocholate in the bile of a dog, sometimes as much as one-third of the whole bile acid salts.[§] Hoppe-Seyler endorses Strecker's statement,[||] which appears to be generally received.

Thenard says of the bile of the pig, that, unlike the bile of the ox, it is a true soap: from it he could obtain no picromel.[¶]

Strecker and Gundelach found in the bile of pigs, as its chief constituent, an acid nitrogenous but free from sulphur, which they called hyocholic acid.* It differs greatly from the glycocholic acid of oxen. It is insoluble in water, and forms with lime and baryta a salt either insoluble or hardly soluble in water. The alkaline salts are thrown down out of their watery solution by chloride of sodium, chloride of ammonium, or alkaline sulphates, a means by which the acid may be had in purity: the formula for the salts is $C^{54}H^{43}NO^{10} + MO$; for the acid $C^{54}H^{43}NHO^{10}$. The acids make up 75 *per cent.* of the solids of pig's bile; and of this about 0·47 *per cent.* is sulphur. There is, therefore, probably a bile acid which has the same relation to hyocholic acid, as taurocholic has to glycocholic.†

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[*] Strecker, *Annalen d. Chemie und Pharmacie*, 1848, Bd. lxvii. p. 46.

[†] Hoppe-Seyler, *Arch. f. path. Anat.* 1858, Bd. xv. p. 132.

[‡] Strecker, *Annalen d. Chemie u. Pharmacie*, 1849, Bd. lxx. p. 178.

[§] George Scott, Beale's *Archives of Medicine*, 1859, vol. i. p. 217.

[||] Hoppe-Seyler, *Phys. Chemie*, Berlin, 1878, p. 289.

[¶] Thenard, *Mémoires de physique et de chemie de la Société d'Arcueil*, 1807, t. i. p. 49.

Hoppe-Seyler thinks that the acids of pig's bile have probably a more complicated composition than the glycocholic and taurocholic acid of other mammals, as he finds they have considerable differences in their influence on the polarised beam, differences which are not always constant. Hoppe-Seyler gives + 2° for hyoglycocholic acid in yellow light, and + 23·62° for hyocholoidic acid, an acid formed by the boiling of hyoglycocholic acid with hydrochloric acid.‡

The bile of a female kangaroo *(Halmaturus)*, was found by Schlossberger to be neutral, and to give a well-marked Pettenkofer's reaction: there were 14·13 *per cent.* of solids, distributed as follows:

Mucus and Colouring Matters . .	4·34.
Cholestearin and Fat	1·09.
Bile Acid Salts	7·59.
Loss and other Salts	1·11.

Very little sulphur (2·47 *per cent.*) was found, so that the bile of the kangaroo is one of the poorest in taurocholic acid yet examined. The bile of the pig, however, contains less sulphur.[*]

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* Strecker and Gundelach, *Annalen d. Chemie und Pharmacie*, 1847, Bd. lxii. p. 205.

† Strecker, *ibid.* 1849, Bd. lxx. p. 179.

‡ Hoppe-Seyler, *Arch. f. path. Anat.* 1858, Bd. xv. p. 139.

Tiedemann and Gmelin are said to be the first who investigated the bile of geese, though from the imperfect state of the chemistry of the bile at that time but little was added to knowledge by their observations.[†] Marsson later on took up the work, and found that the bile in the gall bladders of geese fed on oats contained about 20 *per cent.* of solid matter. He found sulphur very abundant in this bile; and thought that it might turn out to contain a new acid, nearly allied to Strecker's choleic acid, and to this new acid he gave the provisional name of chenocholeic acid. It gives Pettenkofer's reaction.[‡]

Heintz and Wislicenus found a peculiar acid, as Marsson did, in the bile of geese, but they carried their investigations far wider. They found the cholalic acid to be in no way like the ordinary cholalic acid of oxen, or the hyocholalic acid of pigs. Even the shape of the crystals of the soda salt is different. The amount of carbon is much greater, that of oxygen much less, than in the ordinary bile acid, but its formula is homologous with that of hyocholalic acid; the formula of chenocholalic acid is $C^{54}H^{44}O^{8}$ while that of hyocholalic acid is $C^{50}H^{40}O^{8}$.

In the bile of geese these observers have also found another acid, containing sulphur, analogous to taurocholic acid, and which they call tauro-chenocholic acid, as in it chenocholalic acid is combined with taurin. Its formula is $C^{58}H^{49}NS^{2}O^{12}$.[§]

Berzelius seems to have been the first to examine the bile of snakes, of a *coluber* and a *python*;[*] though the results of his observations are not now-a-days of any value to the physiologist. Later on Schlieper examined the bile from the gall bladder of a *Boa annaconda*, and found the ashes after examination to consist chiefly of sulphate of soda, and that the dry residue of the bile held about 6 *per cent.* of sulphur.[†] Schlossberger, in the bile of a *python tigris*, found the same percentage of sulphur, and concludes that in this kind of snake the only bile acid present is the taurocholic in combination with soda.[‡]

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[*] Schlossberger, *Annalen d. Chemie u. Pharm.* 1859, Bd. cx. p. 244.

[†] Tiedemann and Gmelin, *Die Verdauung*, Heidelberg and Leipzig, 1827, Bd. ii. p. 145.

[‡] T. Marsson, *The Chemist*, 1849-50, vol. i. new series, p. 64, abstract from *Arch. der Pharmacie*, 2. Reihe, Bd. lviii. p. 138.

[§] Heintz and Wislicenus, Poggendorff's *Annalen d. Phys. und Chemie*, 1859, Bd. cviii. p. 547.

In the bile of salt-water fish there is seen an exception to the general rule that the bile acids are in combination with soda. Strecker found the acid to be chiefly taurocholic, with very small traces, if any, of glycocholic acid. In the bile of the cod (*Gadus morrhua*) and of the turbot (*Pleuronectes maximus* or *Rhombus maximus*) the chief constituent was taurocholate of potash, while the bile of fresh water fish, such as the pike (*Esox lucius*) and the perch (*Perca fluviatilis*) held much more soda, combined in the bile of the pike with glycocholic acid.[§]

The bile of a species of *Silurus*, taken from a specimen weighing 90 pounds, Schlossberger found neutral and showing a few epithelium cells. It contained 5·52 *per cent.* of solids, composed of 3·63 of bile acid salts, ·23 of fat and 1·48 of mucus and pigment. The salts contained a large amount of sulphur; so that in this case also the bile acid was inferred to be chiefly taurocholic, with a small amount of glycocholic acid.[‖]

Scherer found in the bile of a sturgeon both glycocholic and taurocholic acids.* It gave a well-marked Pettenkofer's reaction.

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[*] Berzelius, Poggendorff's *Annalen d. Physik und Chemie*, 1830, Bd. xviii. p. 87.

[†] Schlieper, *Annalen d. Chemie und Pharmacie*, 1846, Bd. lx. p. 109.

[‡] Schlossberger, *ibid.* 1857, Bd. cii. p. 91.

[§] Strecker, *ibid.* 1849, Bd. lxx. p. 169.

[‖] Schlossberger, *ibid.* 1858, Bd. cviii. p. 66.

The bile contains but very little sulphur as sulphuric acid; and so the amount of sulphur present becomes a means for very nearly estimating the amount of taurocholic acid. Advantage has been taken of this by several chemists in analysing the bile; but unfortunately the later-made experiments vary much from those that are earlier. For example, A. Bensch has found the following amounts of sulphur in the bile of different animals :†

	In 100 Parts.
Oxen.	3·39 — 3·78.
Calf, (before weaning). .	4·88.
Sheep.	5·71.
Goat.	5·20.
Pig, (3 analyses)	0·30. 0·32. 0·36.
Bear.	5·75.
Dog.	6·21.
Wolf.	5·03.
Fox.	5·96.
Domestic Fowl.	4·96.
Fish of different kinds . .	5·52. 5·58.

It has just been said that Schlieper and Schlossberger found 6 *per cent.* of sulphur in the bile of a *boa* and *python* respectively, and that Scherer and Schlossberger found the bile acids of fish to be almost entirely made up of taurocholic acid.

Külz, on the other hand, using Carius' method of estimating the sulphur, finds as follows :‡

	Per Cent.
Bile of Sheep	·189.
„ Man	·136.
„ Swine	·125.
„ Calves	·125.
„ Oxen	·100.

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* Scherer, *Verhandlungen d. phys.-med. Gesellschaft in Würzburg*, 1857, Bd. vii. p. 269.

† Bensch, *Annalen d. Chemie u. Pharm.* 1848, Bd. lxv. p. 194.

‡ Külz, *Arch. f. Anat. Phys.* u. s. w. 1872, p. 106.

Salkowski very properly criticises these results.* A very small amount of bile was used for each analysis, a few milligrammes of sulphates only being obtained; and in this way a large error may creep in if the results be multiplied.

Kunkel also gives ·1 grm. in 100 C.C. of bile as the average for a dog.†

DERIVATIVES OF THE BILE ACIDS.

Cholalic acid, as described above, is a product of the decomposition of both glycocholic and taurocholic acid. It is the non-nitrogenous acid which is common to both, and, by combining with the glycocoll and taurin, forms the special acids of the bile.

Cholalic acid is formed by the decomposition of the bile acids by acids, alkalies, or fermentation. Strecker made it by long boiling of the bile acid salts with baryta. The solution, when allowed to cool, gives a crystalline mixture of hydrate of baryta and cholalate of baryta. This is thrown on a filter, washed with a little boiling water, and then thrown into water acidulated with hydrochloric acid. The cholalic acid separates as a resinous body, and the solution only holds chloride of barium. The fluid, from which the cholalate of baryta was filtered off, is mixed with the washings, and carbonic acid passed through, by means of which the baryta is precipitated as far as may be. The fluid is then heated to boiling, filtered from the carbonate of baryta, and the cholalic acid set free from the baryta by means of hydrochloric acid. A small part of the cholalic acid remains in the carbonate of baryta and may be got by treating it with carbonate of ammonia, and then expelling the cholalic acid with a stronger acid. The cholalic acid is thus obtained in three different fluids. This is the method recommended by Strecker.* Hoppe-Seyler says that the bile should be boiled for 12 or 24 hours with strong potash solution, or baryta solution saturated when hot. The solution should be thrown down with hydrochloric acid, washed with water, dissolved in a little alkali-solution, æther added, precipitated afresh with hydrochloric acid, and then allowed to stand for several days. By the addition of æther the cholalic acid is obtained in crystals. The æther is poured off, the mass pressed, dissolved in hot alcohol, a little water added so that a slight opalescence takes place, and the whole allowed to cool. The cholalic acid forms in tetraëdral crystals,† or, according to Strecker, rarely in quadrate-octaedra. They are colourless, shining, easily broken. They have a somewhat bitter taste, with a scarcely noticeable sweet after-taste.‡ They need 750 parts of boiling, and 4000 of cold, water for solution. They are readily soluble in boiling alcohol, but on cooling separate out. 1000 parts of cold alcohol of 70 *per cent.* keep 48 parts dissolved. Hoppe-Seyler says the crystals are hardly soluble in æther; Strecker that one is soluble in 27 parts of æther.

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* Salkowski, *Centralblatt f. d. med Wiss.* 1872. p. 885.

† Kunkel, *Arch. f. d. ges. Phys.* 1877, Bd. xiv. p. 345.

The amorphous variety, according to Hoppe-Seyler, is like wax and may be kneaded. It is somewhat soluble in water, somewhat more in æther, and very soluble in alcohol.

The formula for cholalic acid is $C^{24}H^{40}O^{5}$. Its rational formula is unknown. The crystals from æther contain 2 molecules of water, those from alcohol 5.

Cholalic acid combines readily with alkalies and drives out carbonic acid from its combination with them. The alkaline salts are all soluble in water: the baryta and lime-salts are with trouble soluble in cold water, but more easily in hot, are very soluble in alcohol. They form fine needles, often stellate. The cholalates of lead and silver are insoluble in water, but soluble in hot alcohol.

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* Strecker, *Annalen d. Chemie und Pharm.* 1848, Bd. lxvii. p. 3.

† Hoppe-Seyler, *Handb. d. phys. u. path. chem. Analyse.* Berlin, 1865, p. 90.

‡ Trifanovsky, (*Arch. f. d. g. Phys.* 1874, Bd. ix. p. 495) says cholalic acid has an intensely bitter taste without any sweet after taste.

Cholalic acid gives Pettenkofer's reaction; it has a dextro-rotatory action on polarised light: +24°·55 for red, and +27°·66 for yellow, light.[*] It dissolves the red blood corpuscles.[†]

Dyslysin, a body noted and named by Berzelius,[‡] is formed by heating cholalic acid to 190° or 200° C. when the acid is split up into dyslysin and water:

$$\overset{\text{Cholalic acid.}}{C^{24}H^{40}O^{5}} - 2\,(H^{2}O) = \overset{\text{Dyslysin.}}{C^{24}H^{36}O^{3}}$$

By boiling with potash, dyslysin takes up water and becomes again cholalic acid. The same decomposition takes place on boiling cholalic acid with acids. A mucilaginous body of a brown colour is separated. This is insoluble in water and cold alcohol; slightly soluble in hot alcohol, soluble in æther. It is not taken up by ammonia or potash; by boiling with alcoholic potash or fusing with potash it is dissolved, and on adding acids a body is thrown down which is no longer dyslysin but choloidic acid.

Choloidic acid, a body first named by Demarçay,[§] has been further investigated by Strecker.[||] At ordinary temperatures it is firm and white, often, however, somewhat coloured. It fuses in boiling water without being dissolved. When dry it fuses at over 150° C.

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[*] Hoppe-Seyler, *Arch. f. path. Anat.* 1858, Bd. xv. p. 138.

[†] Idem, *ibid.* 1862, Bd. xxv. p. 183. Baumstark has published some interesting observations on cholalic acid. (*Berichte d. deutschen chem. Gesellschaft zu Berlin*, 1873, Bd. vi. p. 1185.)

[‡] Berzelius, (*Annalen d. Chemie u. Pharm.* 1840, Bd. xxxiii. p. 147), calls it thus from its difficult solubility: δυς and λύσις.

[§] Demarçay, *Annales de chimie et de physique*, 1838, t. lxvii. p. 198.

[||] Strecker, *Annalen d. Chemie und Pharm.* 1848, Bd. lxvii. p. 22.

The alcoholic solution is made opalescent by water and is acid to litmus. In æther it is only slightly soluble. It is best purified by solution in alcohol and precipitation by æther. It combines with bases and drives out carbonic acid by the aid of heat. The salts of choloidic acid are soluble in water and alcohol, but insoluble in æther.

The weakest acids drive out choloidic acid, even a stream of carbonic acid. The taste is purely bitter, without any sweet after-taste. The formula which Strecker gives is $C^{48}H^{39}O^{9}$, on the old system.

Hoppe-Seyler, however, doubts if this choloidic acid be anything but cholalic.[*] The body which Strecker analysed was probably only a mixture of cholalic acid, dyslysin, and cholonic acid. Like cholalic acid, the body obtained by Strecker's process crystallises in octaëdra and tetraëdra; and the crystals by drying lose 10·2 *per cent.* of water. The formula, after Gerhardt, is $C^{24}H^{40}O^{5} + 2\frac{1}{2}\ H^{2}O$, which equals 9·93 *per cent.* of water. It has much the same action on polarised light as cholalic acid.

Cholalic acid	in alcoholic solution	= + 35°·2.
Acid prepared from dyslysin	,, ,,	= + 35·4.
Cholalate of potash	,, ,,	= + 31·4.
Salt of potash from dyslysin	,, ,,	= + 30·8.

The baryta salt is insoluble in water and thus is distinguished from glycocholic and cholalic acid. Baumstark, on the other hand, believes that a distinct choloidic acid does exist.[†]

Cholonic acid is a nitrogenous derivative from glycocholic acid. If glycocholic acid be added to strong sulphuric acid, the glycocholic acid is dissolved; but if the mixture be warmed, cholonic acid separates, as an amorphous precipitate, which is not soluble in water but is soluble in alcohol. It is not crystallisable. This acid is also formed with cholalic acid when glycocholic acid is boiled with hydrochloric acid. Its formula is $C^{26}H^{41}NO^{5}$. The dextro-rotatory action of cholonic acid is the same as that of glycocholic acid.

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[*] Hoppe-Seyler, *Journal f. pract. Chemie*, 1863, Bd. lxxxix. p. 83.

[†] Baumstark, *Berichte der deutschen chem. Gesellschaft zu Berlin*, 1873, Bd. vi. p. 1187.

Parke did not succeed in getting from taurocholic acid an acid analogous to the cholonic acid derived from glycocholic acid.*

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* J. Parke, Hoppe-Seyler's *Med. Chem. Untersuchungen*, Berlin, 1866, p. 161.

CHAPTER II.

THE BILE PIGMENTS.

THE biliary pigments seem to have been first studied by the illustrious Berzelius,[*] afterwards by Scherer,[†] Hein,[‡] and Heintz.[§] Städeler and Maly have paid special attention to these colouring matters.

The name cholepyrrhin is commonly said to have been given by Berzelius to the orange red pigment of the bile. F. Simon invented a barbarous word, biliphæin,[‖] compounded of Greek and Latin, the use of which has been unfortunately endorsed by Heintz. Dr. Thudichum uses the word cholophæin,[¶] to avoid this bastard word. Städeler called this pigment bilirubin, forming the word with a cognomen like the other names which Berzelius used; biliverdin, bilifulvin, and the like.[**] Maly has continued the use of the name cholepyrrhin.[††] The name bilirubin is so convenient and so commonly used that I shall adopt it in the following pages.

The colouring matters of the bile do not seem to give any absorption bands in the spectrum; as Thudichum,[‡‡]

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[*] Berzelius, *Annalen d. Chemie u. Pharm*, 1840, Bd. xxxiii. p. 139.

[†] Scherer, *ibid.* 1845, Bd. liii. p. 377.

[‡] Hein, *Journal f. pract. Chemie*, 1847, bd. xl. p. 47.

[§] Heintz, Poggendorff's *Annalen d. Physik u. Chemie*, 1851, bd. lxxxiv. p. 106.

[‖] Simon, *(Animal Chemistry*, 1845, Sydenham Soc. Edition vol. i. p. 43,) says that cholepyrrhin was first used by Berzelius, and biliphæin by Simon.

[¶] Thudichum, *Tenth Report of the Medical Officer of the Privy Council*, London, 1868, p. 243.

[**] Städeler, *Annalen d. Chemie u. Pharm.* 1864, Bd. cxxxii. p. 323.

[††] Maly's observations will be found in the publications named below: *Sitzungsberichte d. math.-naturw. Classe d. k. Akademie der Wissenschaften*, Wien 1868, Bd. lvii. Abth. ii. p. 97. *Ibid.* 1869, Bd. lix. Abth. ii. p. 597. *Ibid.* Jahrg. 1874, Bd. lxx. Abth. iii. p. 72: also in *Annalen der Chemie und Pharmacie*, 1872, Bd. clxiii. p. 77. *Ibid.* 1876, Bd. clxxxi. p. 106.

[‡‡] Thudichum, *op. cit.* p. 251.

Preyer,[*] and Vierordt[†] agree. It is only when they are subjected to oxydising agents that these bands make their appearance. Maly noted that a solution of bilirubin in chloroform removed the blue and violet out of the spectrum up to 70; and that even very dilute solutions removed the violet end of the spectrum. Biliverdin in alcoholic solution removed both ends of the spectrum.[‡] Dr. Dalton has described[§] an extreme shortness of the bile spectrum with a band, which he thinks characteristic, at C. This band is best seen in bile which has a distinct green colour; it is not so well seen if the bile be brown or yellow; if bile lose its green colour, the band disappears, but is restored if the green colour be brought back by adding iodine. Dr. Dalton thinks this band to be due probably to the presence of biliverdin. Another band or two may sometimes be seen at D or D 30 E, but never so distinctly as the band at C.

Cholepyrrhin, bilifulvin, or bilirubin, has not been studied much as a product direct from the bile, but as a constituent of gall stones from men or oxen in which it appears in combination with calcium. Maly recommends the gall stones to be broken up, boiled with alcohol and filtered hot. The brown residue on the filter is washed with æther and digested with acetic acid. The acid solution is filtered, and the residue washed with water and alcohol. The remaining powder is now dried and digested for several days in chloroform at the ordinary temperature, or for a few hours in a water bath. The chloroform takes up the pigment, and the bilirubin is obtained by distilling off the chloroform, and washing with spirit. If the pigment be wished for very pure, the whole process had better be repeated once or twice.*

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[*] Preyer, *Die Blutkrystalle*, Jena 1871, p. 187.

[†] Vierordt, *Zeitschrift f. Biologie*, 1874, Bd. x. pp. 44 and 48.

[‡] Maly, *Sitzungsberichte d. math.-naturw. Classe d. k. Akad. der Wissenschaften*, Wien, 1868, Bd. lvii. Abth. ii. p. 106.

[§] Dalton, *New York Med. Journal*, 1874, vol. xix. p. 579.

Städeler recommends another process. The gall stones are digested in æther, and the residue extracted with hot water, dried, and then treated with chloroform. This gives an impure solution of bilirubin. It must be evaporated to dryness and then treated with hydrochloric acid. Carbonic acid is given off, and the violet filtrate contains a great quantity of lime and magnesia. The residue on the filter must be washed and dried, and is then of a dark brown green. To purify it, the bilirubin must be dissolved several times in chloroform, the filtrate evaporated, and the residue washed with æther and spirit. The washings with alcohol are always more or less green, while the bilirubin remains on the filter as an orange-red granular-crystalline powder.

Dr. Thudichum recommends a long and troublesome process. Gall stones from the ox are powdered and made into a dough with a little hot water; an excess of hot water added and the whole well stirred. After standing for several days the fluid is separated by decantation, a process frequently repeated. At last the whole is thrown upon a filter, and the paste left is put into a flask with a large quantity of spirit and boiled. After exhausting the powder with alcohol, it is treated for several days with cold dilute hydrochloric acid. The powder is washed by decantation, lastly on the filter, and a second time with alcohol. After this the powder may be washed with æther, but if the foregoing operations have been properly performed, this last process will be unnecessary. When dried, the powder is boiled with pure chloroform, and exhausted with this liquid. The filtered solution is evaporated, and the residue with absolute alcohol till the latter be nearly colourless, and the residue on the filter red without any admixture of green.†

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* Maly, *op. cit.* p. 96.

† Thudichum, *op. cit.* p. 241.

Heintz appears to be the first who gave a distinct formula for bilirubin.* Scherer and Hein made elementary analyses, but did not succeed in composing a distinct formula. According to Heintz the formula is $C^{31}H^{18}N^2O^9$. Städeler and Maly, however, both give $C^{32}H^{18}N^2O^6$ or in the new notation $C^{16}H^{18}N^2O^3$, and this appears to be generally accepted. Maly believes that bilirubin is the amide of biliverdin which possesses the properties of an acid in uniting with bases.† Dr. Thudichum, however, denies this, and asserts the formula to be $C^9H^9NO^2$.‡

Dr. Thudichum describes two modifications of the red colouring matter of the bile; the one, amorphous, of a bright red colour, which he calls bilirubin; the other, crystalline, of a purple-brown colour, which he calls biliphæin or cholophæin. He regards them as identical chemical substances. The crystals belonged to the rhombic system, "being prisms in some crystallizations, simple, and with nearly obtuse right angles, in others with sharp angles on the one, obtuse angles on the next edge, and planes from secondary prisms cutting off the sharp angles of the primary ones."

Bilirubin heated on platinum foil leaves no residue behind.

Städeler says that amorphous bilirubin is orange coloured; the crystals show the dark red of chromic acid. He finds that good crystals can rarely be got from the solution in chloroform; better are had direct from the bile. Maly describes them as doubly convex, like the section of a biconvex lens.

In water, bilirubin appears to be quite insoluble, slightly in æther, and a little more in spirit. The alcoholic solution made while hot is golden yellow, when

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* Heintz, *op. cit.* p. 114.

† Maly, *Centralblatt f. d. med. Wiss.* 1864, p. 640.

‡ Thudichum, *op. cit.* pp. 241 and 244.

[illegible] filtered the greater part
[illegible] that the filtrate
[illegible] yellowness. Chloroform
[illegible] the more crystal-
[illegible] solution. The chloro-
[illegible] orange colour. A sat-
[illegible] Sulphide of carbon and
[illegible] which Dr. Thudichum
[illegible] only dissolves
[illegible] observer remarks
[illegible] and white of egg;
[illegible] coloured. In
[illegible] it is also a
[illegible] in warm tur-

[illegible] the caustic alka-
[illegible] Städeler
[illegible] in 15000 was
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[illegible] is discussed,
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[illegible] becomes [illegible]
[illegible] brown [illegible]
[illegible]

tion. Maly says that the body remaining on the filter is no longer bilirubin and does not give Gmelin's reaction. This is denied by Städeler, who notes that the red in the play of colours is remarkably fine.

The oxydising action of nitric acid upon bilirubin has long been known as Gmelin's test. Städeler says that a quarter of a milligramme dissolved in 4 C.C. can be readily detected by this means, and that the colours still appear in a solution of one in 70,000 or 80,000. The yellow colour is changed by the action of the acid into green, then blue, violet, ruby red, and lastly dirty yellow. All these stages of oxydation correspond to bodies which can be isolated and preserved. If a solution of bilirubin in chloroform be acted on by a drop or two of nitric acid, and spirit added as soon as the blue or violet colour appears, the solution becomes deep blue and remains so. In the same way a fine green or red can be had, according to the time at which the spirit of wine is added. Heynsius and Campbell have made a special study of the spectra of these bodies.[*]

The derivatives of the bile pigments cannot be more than mentioned here, as their discussion would in most points be foreign to the object of this work. Their history begins with Städeler, who has the merit of being the first to point out the kindred of the blue product of the oxydation of bilirubin with the indigo colouring matter of the urine.[†] In 1869 Jaffe named the colouring matter of the urine urobilin, because he believed it to be a derivative of the bile pigment, whether by oxydation or not was left undetermined.[‡] Heynsius and Campbell believe it to be due to oxydation;[§] Maly, however, to reduction.* Vanlair and Masius describe another derivative, found in abundance in the fæces, which is closely allied to urobilin, and which they name sterco-bilin.†

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[*] Heynsius and Campbell, *Arch. f.d. ges. Phys.* 1871, Bd. iv. p. 497.

[†] Städeler, *op. cit.* p. 333.

[‡] Jaffe, *Arch. f. path. Anat.* 1869, Bd. xlvii. p. 423. See also *Arch. f. ges. Phys.* 1868, Bd. i. p. 262. Magendie (*Précis élém. de Phys.* Paris, 1836, 4e éd. t. ii. p. 474, note) conjectures: Il est probable que la matière jaune de la bile est aussi celle qui colore le sérum du sang, l'urine etc.

[§] Heynsius and Campbell, *loc. cit.*

The relation of the bile pigments to the colouring matters of the blood is that which has the greatest attraction for the physician, inasmuch as much of the doctrine of hæmatagenous jaundice depends upon the belief that the two bodies are the same. Doubtless the idea that hæmatoidin and bilirubin are identical has much to recommend it to the notice of physiological chemists, but the notion has, I think, been asserted with scarcely sufficient proof. It is, however, an example of the rashness which characterises the present generation of physiological chemists; they make up for the extreme uncertainty of their opinions by an increased boldness of assertion.

Saunders, more than 80 years ago, thought that there might be some relation between the colouring matters of the blood and the bile pigments.‡ Frerichs, in his essay on the chemistry of human bile, makes the short remark that the colouring matters are allied on one side to hæmatin and on the other to black pigment;§ but two years later Virchow, in the midst of his well-known work on the pathological pigments, opened the question of the relation of the bile colouring matter to the blood. Speaking of the red sealing-wax like matter which is so often found in echinococci cysts in the liver, he says that, in cases where this matter had undoubtedly had its origin in bile, he had found the crystals on the wall of the cyst very like those of old blood clots. Some of these crystals he attempted to examine chemically; but naturally the tests could not be very satisfactorily applied with so small a quantity, and with such impure materials. He found the crystals insoluble in æther, alcohol, or alcohol containing sulphuric acid, or turpentine. No change took place with chlorine vapour, while old *corpora lutea* were completely bleached. Both were acted on by sulphide of ammonium, the crystals remaining unchanged, while the *corpora lutea* became black. With nitric acid they quickly became brown-red, then intensely green, blue, and rose coloured. The crystals were soluble in alkalies. Virchow thinks these observations make it very probable that blood colouring matter may be changed into bile pigment.*

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* Maly, *Annal. d. Chemie. u. Pharm.* 1872, Bd. clxiii. p. 77. He has named the last product of oxydation choletelin, from τέλος, end. *Sitzungsbb. d. math.-naturw. Classe d. k. Akad. d. Wiss.* Wien, 1869. Bd. lix. Abth. ii. p. 605.

† Vanlair and Masius, *Centralblatt f. d. med. Wiss.* 1871, p. 369. See also Stokvis, *ibid.* 1872, pp. 3 and 785, and 1873, p. 211; and *Journal of the Chemical Society*, 1872, vol. xxv. p. 308, and 1873, vol. xxvi. pp. 78 and 288. Vierordt, *Zeitschrift f. Biologie*, 1873. Bd. ix. p. 160, and 1874, Bd. x. p. 21.

‡ Saunders, *A Treatise on the Structure, Economy, and Diseases of the Liver*, London, 1803, third edit. p. 147. "Green and bitter bile being in common to all animals with red blood, and found only in such, makes it probable that there is some relative connexion between this fluid and the colouring matter of the blood, by the red particles contributing more especially to its formation." Cf. p. 160.

§ Frerichs, *Hannoversche Annalen*, 1845, Jahrg. v. p. 145.

Robin also gave great help to Virchow's notions. A mass, weighing 3 grammes, of the red colouring matter taken from hydatid cysts of the liver, was found to consist entirely of very regular crystals, quite like those described by Virchow. They were completely dissipated by heat and were insoluble in water, alcohol, æther, glycerine, and acetic acid; but soluble in ammonia; nitric acid quickly dissolved the crystals with effervescence, leaving a red solution; sulphuric acid did not dissolve them, but they became greenish. Robin thought the mass had its source in extravasated blood. An elementary analysis gave the following results:

	I.	II.	III.
Carbon	65·046.	65·851.	
Hydrogen	6·37.	6·465.	
Nitrogen			10·5050.
Oxygen	18·0888.	17·1788.	
Ashes	00·0002.	00·0002.	

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* Virchow, *Arch. f. path. Anat.* 1847, Bd. i. p. 427.

Städeler and Maly give as the percentage of their analyses of bilirubin, the following figures:

	STÄDELER.[*]	MALY.[†]
Carbon	67·15.	67·16.
Hydrogen	6·.27	6·20.
Nitrogen	9·59.	
Oxygen	16·99.	

The percentage analyses of these two bodies, therefore, correspond in many particulars. Robin compares his analysis with one of Mulder's, of hæmatosin, and appears to think that the substance analysed was a derivative of the blood, without the iron salts. He remarks that the amount of blood extravasated in this cyst must have equalled 1800 grammes at least in order to furnish this quantity, 3 grammes of colouring matter.[‡] It is hard to see how so much blood can have been poured into the cyst, but it is easy to understand that a great deal of bile might have found its way into the sac; it is common to find this red sealing-wax like stuff in cysts communicating with the bile ducts. Virchow's opinion[§] that this red matter had its source in the bile would seem to be correct. It is very likely that Robin analysed only an impure bilirubin. Städeler points out that Robin's formula, $C^{14}H^{9}NO^{3}$, is not justified by the analysis, but that $C^{30}H^{18}N^{2}O^{6}$ would be more correct; the hydrogen only in this case being ·1 and ·2 *per cent.* less than found.[||]

Zenker and Funke say that bilifulvin, that is, bilirubin, either spontaneously or by treatment with æther, changes into fine large crystals which shew "all the properties" of hæmatoidin, and are therefore identical with it.* It would be, however, interesting to know what "all the properties" of hæmatoidin are.

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[*] Städeler, *Annalen d. Chemie u. Pharmacie*, 1864, Bd. cxxxii. p. 328.

[†] Maly, *Sitzungsberichte der math. wiss. Classe der k. Akad.* Wien, 1868, Bd. lvii. Abth. ii. p. 97.

[‡] Robin, *Comptes rendus*, 1855, t. xli. p. 506.

[§] Virchow, *loc. cit.*

[||] Städeler, *op. cit.* p. 348.

Jaffe examined an old hæmorrhage into the brain with a view to getting bilifulvin from it. It was dried in a water bath, cut up fine, and extracted with chloroform, after being first moistened with a little alcohol. The extract becoming of a deep yellow colour: the chloroform was then distilled until but a few drops were left, and these were allowed to evaporate spontaneously in a watch-glass. This should be carried on in the dark, in order to hinder oxydation. The crystals left after this evaporation were golden yellow in colour, and remarkably fine; they corresponded closely in shape to those of hæmatoidin. Jaffe, wishing to free them from fat, found a good number of them soluble in æther. The remainder was easily soluble in carbonate of soda. The yellow solution became green during filtration. A small residue was lastly treated under the microscope with nitric acid. The crystals shewed the well-known reaction of bile pigment, becoming first green, then blue. Jaffe had no longer any doubt that by simple recrystallization of hæmatoidin, bilifulvin can be had: therefore that the two bodies are identical. It must be, however, noted, that Jaffe confesses that he was unable to obtain bilifulvin from other old hæmorrhages which had lain long in spirit.†

Hoppe-Seyler found in the fluid from a cyst in the breast, crystals, which from their crystallisation and reaction with nitric acid he judged to be the same as bile pigment, and yet from the source, as in Jaffe's, could not have had their origin in the bile.‡

Valentiner is said to have made some observations which favoured the belief that hæmatoidin and bilirubin are identical, finding crystals of the same shape as hæmatoidin in an extract of bile with chloroform. I have not, however, been able to see the journal[*] in which the paper was published, so that I can give no trustworthy account of its contents.

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* Funke, *Lehrbuch d. Physiologie*, Leipzig, 1860, 3te Aufl. Bd. i. p. 246.

† Jaffe, *Archiv f. path. Anat.* 1862. Bd. xxiii. p. 192.

‡ Hoppe-Seyler, *ibid.* 1862, Bd. xxiv. p. 10.

Städeler, criticising Valentiner's work, says that he has always found the crystals of bilirubin to be less perfect, as the solution out of which they form approaches purity. If bile be shaken up with chloroform, as in Valentiner's work, and the chloroform allowed to evaporate, there form orange coloured elliptic tables, or very small, almost right angled, tables, the angles of which are very different from those of hæmatoidin.

The results were the same in nearly every case, the rhomboid forms were always recognised, with some slight changes in the sides and angles in which the diagonals of the rhomboids were marked by changes of colour. Only as an exception were seen forms which approached the ordinary hæmatoidin appearance. Städeler also found that the crystals which formed out of benzol and sulphide of carbon solutions showed greater resemblance to hæmatoidin; hæmatoidin has never convex surfaces, while these are commonly seen in bilirubin crystals, so that at first sight they may be mistaken for uric acid.[†]

The important point, however, is the analysis, and it would seem that an analysis of hæmatoidin has yet to be made. Holm, under Städeler's guidance, and in his laboratory at Zürich, has attempted a further study of the differences between hæmatoidin and bilirubin.[‡] He first tried to win from old hæmorrhages in the brain a sufficient amount of hæmatoidin by means of extraction with chloroform. He found, however, that but very little could be had in this way. He noted, however, as Salkowski has done, that the yellow colour of the chloroform extract changed by exposure to the light into a bright green. The next attempt was on the *corpora lutea* of cows, in these good crystals were rarely met with. The hæmatoidin was extracted by chloroform or sulphide of carbon, from which it could readily be obtained in crystals. The crystals were found to be acute angled triangular tables, of which one side is convex; this convex side can be replaced by two straight lines whereby the tables become somewhat of the shape of a delta. Two of these triangular tables may be joined so as to present the appearance of the ordinary rhombic crystals of hæmatoidin.

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[*] Valentiner, Günsburg's *Zeitschrift f. klin. Med.* 1858, p. 46.

[†] Städeler, *op. cit.* p. 344.

[‡] Holm, *Journal für praktische Chemie*, 1867, Bd. c. p. 142.

It has been said that hæmatoidin is soluble in æther and sulphide of carbon. In absolute æther it is less soluble than in these. It is not soluble in absolute alcohol or water, nor in ammonia or soda. Acetic acid (glacial) dissolves it when warmed, and if to this solution a drop of ordinary nitric acid be added, the mixture becomes blue, but this colour immediately disappears, and the solution remains colourless. The solution of hæmatoidin in chloroform gives no Gmelin's reaction with nitric acid, nor even the blue colour just spoken of: the colour of the yellow solution is simply discharged.

Holm sums up: Bilirubin and hæmatoidin have not only different forms and colours but different chemical properties. The former shows the properties of a weak acid; the latter is indifferent.

Bilirubin is soluble in sulphide of carbon with a golden yellow colour; hæmatoidin with brilliant red.

Bilirubin is insoluble in æther; hæmatoidin soluble.

Bilirubin is readily soluble in alkalies; hæmatoidin insoluble.

Salkowski, however, suffers not this statement of Holm's to go undenied. The contents of a thyroid cyst were obtained by puncture during life. The mass showed all the appearances of bilirubin. Under the microscope good rhombic tables were seen which were readily soluble in chloroform with golden yellow colour, and a little also in æther. Both these solutions readily gave up this body when shaken with a weak soda solution, while the chloroform or æther became colourless. The alkaline solution gave the well-known Gmelin's reaction with nitric acid, and not merely a rapidly disappearing blue, as Holm found with his hæmatoidin solutions. Exposed to the air the solutions became green.

Salkowski confesses, however, that the body which he extracted was so small in amount that it was only enough to make out these foregoing properties.*

Preyer, so well known for his researches on the blood crystals, is very strongly of opinion that bilirubin and hæmatoidin are not identical. He finds the spectrum of the two bodies entirely different. The chloroform extract of gall stones shows in the most dilute, as well as in the most saturated solutions, no absorption bands from A to G. With increased concentration, the refrangible part towards the green gets more and more dark without showing bright intervals.

Now the hæmatoidin extracted by chloroform from the *corpus luteum* of the cow, in which Preyer noted abundance of hæmatoidin crystals, behaved quite differently. The yellow chloroform extract gave a characteristic spectrum; a well-marked absorption band between b and F, close to F, and a smaller one between F and G. If the concentration were increased, an absorption band appeared between 80 and 115, while red, orange, yellow, and green remained bright.

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* Salkowski, *Medicinisch-Chemische Untersuchungen*, herausgeg. von Hoppe-Seyler, Berlin, 1868. Heft iii. p. 436.

Preyer found the same spectrum in hæmatoidin crystals from an old hæmorrhage into the brain; so that it is not another body, taken up from the *corpus luteum* by the chloroform which gives the two bands. Another reason that bilirubin is different from hæmatoidin is the great colouring power of the former, which the latter does not possess. Also in æther containing fat, hæmatoidin is soluble, while bilirubin is not, as Preyer has convinced himself.[*]

Thudichum, however, asserts that the body which Holm, Preyer, and other observers have examined is not hæmatoidin but lutein; and that lutein differs altogether from bilirubin, or as Thudichum calls it, cholophæin.[†] The lutein of Thudichum appears to resemble the luteo-hæmatoidin or hæmolutein of Piccolo and Lieben.[‡]

In conclusion, it may be observed that there are at present scarcely sufficient data for the formation of a trustworthy opinion that bilirubin and hæmatoidin are identical. The shape of the crystals, the presence of iron, the solubility in various reagents, are given differently by different observers.

Kühne[§] and Hoppe-Seyler[‖] boldly cut the knot by using hæmatoidin as a synonym for bilirubin; but if the observations of Preyer on the spectrum of the two bodies be in any way trustworthy, it will hardly be possible to continue this assertion. All observers who have examined the spectrum of bilirubin announce it to be free from absorption bands; but even the hæmatin free from iron shows according to Hoppe-Seyler four absorption bands in the red, yellow, and green.[*] The balance of evidence is in my opinion against the identity of the two bodies.

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[*] Preyer, *Die Blutkrystalle*, Jena, 1871, p. 188.

[†] Thudichum, *Proceedings of the Royal Society of London*, 1869, vol. xvii. p. 255.

[‡] Piccolo and Lieben, *Giornale di scienze naturali ed economiche*, Palermo, 1866, vol. ii. p. 258.

[§] Kühne, *Lehrb. d. phys. Chemie*. Leipzig, 1866, p. 72.

[‖] Hoppe-Seyler, *Handb. d. phys. und path. chem. analyse*, Berlin, 1865, p. 161.

Bilirubin enters readily into combination with bases[†] and these combinations for the most part are insoluble in water, spirit, æther, or chloroform. The best known combination is that with calcium so often met with in gall stones. It may be prepared by decomposing a weak ammoniacal solution of bilirubin with chloride of calcium; the bilirubin-calcium is thrown down as a dark red precipitate. Its formula according to Städeler, who wrote in the præ-Gerhardtian days, is $C^{32}H^{17}CaN^{2}O^{6}$: or according to the modern notation $C^{16}H^{17}CaN^{2}O^{3}$. According to Maly, bilirubin is the amide of biliverdin which possesses the properties of an acid.[‡]

Biliverdin. The name biliverdin was first used by Berzelius who thought this green pigment of the bile of herbivorous animals allied to the vegetable chlorophyll.[§] Heintz[‖] first gave it a formula $C^{16}H^{9}NO^{5}$; Maly, however, gives a formula $C^{16}H^{18}N^{2}O^{4}$ which differs from that above in containing less oxygen.[¶] It would appear from this latter that biliverdin is only bilirubin with one atom of oxygen more, as is seen by the following equation, $C^{16}H^{18}N^{2}O^{3} + O = C^{16}H^{18}N^{2}O^{4}$. Städeler assumes that bilirubin takes up water as well as oxygen in becoming biliverdin and adds two molecules of water to the formula: but this theory is confessedly founded upon the analysis by Heintz of an impure biliverdin, so that in this matter Maly's formula should be received rather than Städeler's.

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[*] Hoppe Seyler, *Arch. d. path. Anat.* 1864, Bd. xxix. p. 235.

[†] Thudichum (*Tenth Report* &c. Lond. 1868, p. 244), gives a full account of these.

[‡] Maly, *Centralblatt f.d. med. Wiss.* 1864, p. 640.

[§] Berzelius, *Annalen d. Chemie*, 1840, Bd. xxxiii. pp. 140 and 177. Biliverdin has been called by Dr. Thudichum cholochlorine (*Tenth Report of the Medical Officer of the Privy Council*, 1868, London, p. 249.) This attempt to disturb the old name is to be regretted, as no good object can possibly be attained. See also Thudichum, *Journal of the Chemical Society*, 1876, vol. ii. p. 27.

[‖] Heintz, Poggendorff's *Annalen d. Physik u. Chemie*, 1857, Bd. lxxxiv. p. 117.

[¶] Maly, *op. cit.* 1868, Bd. lvii. Abth. ii. p. 105. See also the same *Sitzungsberichte*, Jahrg. 1874, Wien, 1875, Bd. lxx. Abth. iii. p. 72.

Dr. Thudichum gives the formula $C^8H^9NO^2$ and thinks that biliverdin arises from bilirubin by the addition of 2 atoms of oxygen and subtraction of one of carbonic acid.

Maly says that there are three sets of reagents by means of which bilirubin can be converted into biliverdin: acids, alkalies, and bromine and iodine.

Maly finds that the action of acetic acid and chloroform upon bilirubin, in sealed tubes, and aided by the heat of a water bath, is to change the bilirubin, into a green body. The change of colour is complete, and no other reaction shows it so well. Other acids, as hydrochloric, heated with bilirubin, cause the formation of a green body. Phipson has recommended the use of strong sulphuric acid for this purpose.* Maly found that anhydrous sulphurous acid did not change bilirubin into biliverdin, when heated in sealed tubes in a water bath: the alcoholic solution remained pure golden yellow. This seemed to show that the oxygen comes from the air, not from the acid, as in presence of sulphurous acid there could scarcely be oxydation of a second body.

Also with alkalies, Maly found that if bilirubin were dissolved in dilute soda solution, and one half put in a tube above mercury, the other left open in a dish to the air, the portion left open to the air became brown green in a few days, while the portion cut off from the air retained its red brown colour at the end of a month. If a few bubbles of oxygen were now allowed to enter the tube with the quicksilver, they were gradually absorbed and the fluid became green.

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* Phipson, *Journal of the Chemical Society*, 1867, vol. xx. p. 458.

Another solution of bilirubin in weak soda was poured into a U tube with one end sealed, and the sealed end completely filled with the fluid. Here one end only of the fluid was exposed to the air; and if the green colour were due to oxydation from the air, the colour would first appear at that end which was exposed and gradually spread by the bent part into the closed tube. This was really the case.

In another experiment Maly introduced dry bilirubin into a strong glass tube within which were a few glass globules with thin walls containing dilute soda solution. The glass tube was drawn out into a fine capillary nozzle, bent into a U shape. The glass tube and its contents were now raised by means of a water bath to the temperature of 23·1° C. The capillary tube was then quickly sealed with the blow-pipe. The globules were now broken, and in a few days the fluid became green. The tube was then again heated to 23·1° and the end of the capillary tube broken off under water. Water immediately found its way through the capillary tube into the glass.

These experiments show that the oxygen in the formation of biliverdin is derived from the air. Indigo white, gallic acid, and pyrogallic acid behave in this way just as bilirubin does.*

Besides the acids and alkalies, Maly finds that bromine and iodine have also an action upon bilirubin, bromine especially so. If bilirubin be introduced into a bell jar in which moist air and bromine gas are present, the bilirubin soon becomes dark, and no longer soluble in chloroform, but is soluble in spirit with a pure green colour. The action of the bromine may very easily go too far, so it is better to use the following method: a yellow solution of bilirubin in chloroform is mixed with a few drops of a very weak alcoholic solution of bromine.

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* Maly, *Wien. Sitzungsbb.* 1868, Bd. lvii. Abth. ii. p. 99.

The first few drops make the fluid dark green, and the fluid must be carefully added in order to hit the point at which the whole fluid becomes a fine green.

Nascent oxygen has a rapid action upon bilirubin. If a little binoxyde of lead be carefully added to, and mixed with, a freshly prepared alkaline solution of bilirubin, the fluid acquires, before two minutes be over, the green brown colour which bilirubin has after it has simply stood exposed to the air for a few days. If a little hydrochloric acid and much spirit be added, there is at once a solution of biliverdin.

Spongy platinum lessens the time of the formation of biliverdin from a few days to a few hours. If the red brown solution of bilirubin be placed in a shallow dish, and spongy platinum thrown in, it is possible to see the change of colour pass from the platinum into the fluid around.

Permanganate of potash gives at once further oxydation products.

According to Maly the best method of preparing biliverdin is as follows: Binoxyde of lead is slowly mixed with an alkaline solution of bilirubin until the fluid give a pure green precipitate with acids. The whole of the fluid is then faintly acidified with acetic acid, when there is a complete precipitation of biliverdin-lead, leaving the fluid colourless above. The precipitate is filtered off, washed till the filtrate be free from lead, then acted on by alcohol holding sulphuric acid, filtered and washed with water.

Pure biliverdin is a black shining body, but when powdered is black green. It is without taste or smell and does not readily become wet with water. When heated to 100° C. it gives up some amount of water. At this temperature it remains unchanged in weight, but after being thus dried becomes very hygroscopic.

The purest biliverdin is soluble in alcohol. The solution is not deep green, but rather sap green. As soon, however, as a trace of acid be added (hydrochloric, sulphuric, or acetic) the whole becomes of a fine green.

If to the alcoholic solution of biliverdin a little ammonia and chloride of calcium be added, a dark green precipitate, insoluble in water, is thrown down: if nitrate of silver be added, a dark brown precipitate is thrown down in flakes, with complete decoloration of the fluid. This biliverdin-silver is not soluble in water, but is easily soluble in ammonia with dark chestnut colour. Biliverdin-lead prepared in the same way is in brown green flakes.

Rubbed up with concentrated sulphuric acid, biliverdin is dissolved with a green colour, and is thrown down unchanged by water, in green flakes which are soluble in alcohol.

In caustic alkalies and their carbonates, it is dissolved with a sap green or brown green colour. It is soluble in small amount in æther, and not in chloroform. If, however, the chloroform hold a little alcohol, it dissolves the biliverdin readily. It is also soluble in glacial acetic acid, in chloroform and glacial acetic acid mixed, and also in ordinary strong acetic acid, with remarkably fine colour.

Biliverdin is not soluble in benzol, sulphide of carbon, very slightly soluble in amylic alcohol and iodine-æthyl, but if these two bodies contain a little æthylic alcohol, they dissolve biliverdin with ease.

Methylic alcohol dissolves biliverdin as readily as ordinary alcohol.*

Bilifuscin. It seems to be agreed by all chemists that bilirubin and biliverdin are present in the bile, and are the chief colouring matters of the secretion. Städeler, however, describes a series of pigments, the existence of which is not admitted by others. One of these pigments is bilifuscin, which Städeler finds in the dark brown green residue which is left in his method after the action of hydrochloric acid upon the bilirubin from gall stones. (See page 28.) Boiling chloroform dissolves the bilirubin, and the extracts are at first dark coloured, and leave by evaporation a very dark residue, which liquifies in the heat of a water bath, and becomes crystalline on cooling. If this mass be treated with absolute alcohol, a brown pigment, with other matters, is extracted. This brown pigment Städeler calls bilifuscin. To obtain it out of the alcoholic solution, the fluid is evaporated to dryness, and the black brown residue treated with absolute æther. The æther takes up a part of the pigment and the palmitic acid and other fatty acids. The bilifuscin, insoluble in the æther, is found to be scarcely soluble in chloroform. It is an almost black, shining, brittle body, which in powder is almost olive green.

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* Maly, *Sitzungsberichte d. math.-naturw. Classe d. kaiserlichen Akademie*, Wien, 1868, Bd. lvii. Abth. ii. p. 104.

With nitric acid it gives the same play of colours as bilirubin. From the elementary analysis, Städeler gives the formula: $C^{32}H^{20}N^{2}O^{8}$, on the old notation. It is therefore, only bilirubin with two more molecules of water. After incineration it leaves no ashes.

When much diluted, the solution in alcohol shows the same colour as deeply jaundiced urine. It appears to be almost insoluble in æther, chloroform, and water. It appears to be soluble in alkaline solutions and to form a compound with lime as bilirubin does, but much less bulky.*

If bilirubin be heated with hydrochloric acid, a dark brown appearance is formed, due, Städeler thinks, to the presence of his bilifuscin.†

Biliprasin. Städeler's second pigment, biliprasin, is got when the residue from the gall stones gives no longer any brown pigment, and acquires a bright olive colour. It still contains much bilirubin, and also a green colouring matter, biliprasin, which dissolves in alcohol with a fine green colour. It is removed by repeated treatment with spirit, and then the bilirubin completely extracted with boiling chloroform. To prepare the biliprasin from the alcoholic solution, which also contains a very small amount of bilirubin, the solution must be evaporated to dryness, and the residue powdered and treated with æther and chloroform. It must then be dissolved in a very little cold spirit, and the filtered deep green solution evaporated to dryness. The pure biliprasin remains as a shining, almost black, brittle crust, like bilifuscin; when powdered it has a greenish-black colour. It becomes fluid on being heated, shows bubbles and sends off peculiarly smelling vapours which are but little coloured. When incinerated it leaves about 0·6 *per cent.* of ashes of weak alkaline reaction but not effervescing with acids. The formula according to Städeler is $C^{32}H^{22}N^{2}O^{12}$ on the old notation.

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* Städeler, *Arch. d. Chem. u. Pharm.* 1864. Bd. cxxxii. pp. 326 and 337.

† Städeler, *ibid.* p. 334.

Very little biliprasin is found in gall stones. It is insoluble in water, æther, and chloroform, while it is easily soluble in alcohol with green colour. The solution of biliprasin becomes brown with ammonia, and this distinguishes it from biliverdin. It gives a fine play of colours with nitric acid; it is easily soluble in the pure alkalies, but less in the carbonate of soda. If acids be added to the alkaline solution, the green colour returns, and the solution is no longer brown. This reaction is seen in jaundiced urine. Städeler thinks that the colour of this urine is due chiefly to biliprasin.[*]

Bilihumin is the body which remains behind when the gall stones have been treated with æther, water, dilute acids, chloroform, and spirit. In order completely to free it from the pigments spoken of above, it is washed with ammonia water, and remains as a black brown powdery body. Städeler made no elementary analysis of it for it still contains epithelium and mucus, and is therefore impure. It shows a play of colours with nitric acid.

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[*] Städeler, *Annalen d. Chemie*, 1864, Bd. cxxxii. p. 339.

Blue pigments have been mentioned by several chemists when treating of the constitution of the bile. Städeler, in speaking of the products of the oxydation of bilirubin, pointed out that a blue pigment could be got as one of the stages, and thought it probable that this blue pigment had some relation to the indigo colouring matter of the urine.* Maly likewise described more in detail the blue product of the oxydation of bilirubin.†

Ritter has described a blue pigment in the bile of man, oxen, sheep, pigs, dogs, and cats, and which he isolates by the following process: the bile is filtered and shaken with chloroform; the chloroform is separated by decantation, and then shaken up with a weak solution of soda; this is afterwards neutralised with hydrochloric acid; the two layers are separated, the watery holding the blue matter in suspension. This blue pigment is insoluble in chloroform or acids. Its alkaline solution is colourless or yellow. The only difference between the new body and indigo is, that the solution of the former in an alkaline glucose fluid, if neutralized by an acid and exposed to the air, does not allow a red compound to be deposited until a few days be over, or even as much as a month; while in like solutions of indigo the colour becomes immediately blue.‡

Jaffe also says that if the impure solution of bilifuscin, which is obtained when the chloroform extract of gall stones is acted on by absolute alcohol, be acidified and exposed to the sunlight, the solution, at first of a dirty brown, passes in an hour or two into a fine blue, and this without any intermediate stage of green. It shows three absorption bands in the spectrum, but Jaffe has not had an opportunity for further study of the body.[*]

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* Städeler, *op. cit.* p. 333.

† Maly, *Sitzungsberichte d. math.-naturw. Classe d. k. Akad. d. Wissenschaften*, Wien, 1869, Bd. lix. Abth. ii. p. 601.

‡ Ritter, *Bulletin mensuel de la Société chimique de Paris*, 1870, t. xiii. p. 212.

Bilicyanin. Heynsius and Campbell have described the changes which the spectrum of the bile pigments undergoes in oxydation. They find that all the pigments which Städeler describes give, when oxydised, a violet blue pigment which at first shows bands at C and E, later only one band at F. The place of this band, therefore, agrees with that described by Jaffe. The same body arises also by the action of other oxydising agents, and it was possible to obtain the body in substance by treating bilirubin with bromine water, washing with water, shaking up with chloroform, and evaporation of the extract. Heynsius and Campbell called this new body bilicyanin on account of its deep blue colour. It appears that Stokvis had before them described a body identical with this, but named it choleverdin;[†] he has, however, withdrawn this name, and now uses only bilicyanin.[‡] Heynsius and Campbell find that if the oxydation of bilirubin by means of nitric acid be allowed to proceed so far that only the band at F be visible, and if then the solution be thrown into a large amount of water, brown flakes of choletelin are thrown down. This body in acid solutions shows the band at F; in alkaline solutions it does not immediately show the band described by Jaffe and marked with d, but it does show it after the addition of chloride of zinc, without the exhibition of fluorescence. This choletelin they consider identical with the urobilin of Jaffe.

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[*] Jaffe, *Arch. f. d. ges. Phys.* 1868, Bd. i. p. 271.

[†] Stokvis, *Maandblad v. h. Genootsch. ter bevord van nat.- gen.- en heelk. te Amsterdam*, 1870. s. 10. I have not seen this article. I borrow the reference from Heynsius and Campbell.

[‡] Stokvis, *Journal of the Chemical Society*, 1873, vol. xxvi. p. 288.

Bilicyanin they always find in human gall stones, when these are boiled with hydrochloric acid after complete exhaustion with solvents. It is never found in fresh bile, but is formed quickly in the alcoholic extract by standing exposed to the air. Choletelin was found in two gall stones, very often in jaundiced urine; bilicyanin, however, was found only once and that but for a short time.*

Dr. Thudichum has given many spectra of derivatives ot the colouring matters of the bile, which he describes and names. The reader is referred to his work for further information.† Likewise Städeler at the end of his essay describes certain green colouring matters which give a decided Gmelin's reaction.‡

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* Heynsius and Campbell, *Centralblatt f. d. med. Wiss*, 1872, p. 696.

† Thudichum, *Tenth Report of the Medical Officer of the Privy Council*, Lond. 1868. p. 251.

‡ Städeler, *op. cit.* p. 348.

CHAPTER III.

THE FATS, SALTS, GASES, AND OTHER CONSTITUENTS OF BILE.

CHOLESTEARIN, though found in the bile, is not peculiar to it as the bile acids are, but it is found widely distributed in various other parts and fluids of the body. Full descriptions of it may be found in the chemical handbooks, and I shall therefore not attempt to give an exhaustive account of its chemistry.*

The most common method of preparing cholestearin is from gall stones, which ordinarily contain a large amount of this body. They are powdered and then extracted with boiling alcohol, the solution being filtered while hot. On cooling, the cholestearin separates in crystals, which must be purified by being dissolved in boiling alcoholic solution of potash, allowed to separate on cooling, and again washed with cold alcohol and water. Last of all they must be again dissolved in alcohol and æther, and the solution allowed to evaporate to crystallization. In this way cholestearin may be got from the alcohol and æther out of which the bile acids have crystallised.

Cholestearin is insoluble in water, but soluble in boiling alcohol, in æther, chloroform, and benzol. It crystallises from alcohol in flat rhombic tables; from chloroform, benzol, and æther, in anhydrous shining fine needles. The flat tables often need a very fine opening in the stage of the microscope to allow them to be seen.

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* A name was first given to the crystalline principle of gall stones by Chevreul (*Annales de Chemie et de Physique*, 1816, t. ii. p. 346.) He called it *cholesterine*, from χολή bile, and στερεός solid. To my mind a better name is cholestearin, from χολή, bile, and στέαρ, fat, as it is by no means the most important part of the solids of the bile, but is only the fat of the bile. The Germans formerly spelt the word in this way. Of late they have followed the French.

The formula for cholestearin is $C^{26}H^{44}O^{2}$. It was shown by Berthelot to be a monatomic alcohol.[*] The olefiant gas of the series is cholestearilin, $C^{26}H^{42}$; obtained by the action of strong sulphuric acid on cholestearin.

Cholestearin fuses at 145° C. and can be sublimed in sealed tubes without change at 360°C. Solutions of cholestearin have a levo-rotatory action on polarised light, for yellow light, −34°; for red, −27°·5; for white, −39°·5.[†]

Although cholestearin be insoluble in water, yet it is held in solution in the bile by the action of the alkaline salts of the bile acids, which, like soaps, are able to dissolve cholestearin.

With strong sulphuric acid and iodine a violet colour is given; with chloroform and sulphuric acid, a blood-red colour, changing to purple.

Lecithin, a body containing phosphorus, is also found in the bile. Like cholestearin it is not peculiar to the bile, but is found in greater abundance in the nervous tissues. By some it has been thought akin to Oscar Liebreich's protagon. It is also found in the yolk of egg, semen, white corpuscles, and serum, accompanied by cholestearin.

After yolks of egg have been freed from fat and cholestearin by means of æther, they are extracted with warm absolute alcohol. This alcoholic extract is concentrated and then exposed to a cold of −10°C. A precipitate is thrown down of lecithin. Another method is to throw down the alcoholic solution of lecithin with chloride of platinum with which it forms crystals.

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[*] Berthelot, *Annales de Chemie et de Physique*, 1859, t. lvi. p. 51.

[†] Hoppe-Seyler, *Arch. f. path. Anat.* 1858, Bd. xv. p. 129.

Lecithin is a yellowish mass, not crystalline, and very hygroscopic; though insoluble in water, it swells up in water and becomes white and milky. It is insoluble in acids and alkalies, and chloride of sodium. Æther dissolves it easily; cold alcohol, a little; hot, readily.

By boiling with baryta water, lecithin is decomposed into neurin or cholin, glycerine-phosphoric acid, and stearate of baryta:

$$\overset{\text{Lecithin.}}{C^{44}H^{90}NPO^{9}} + 3(H^{2}O) = \overset{\text{Stearic Acid.}}{2(C^{18}H^{36}O^{2})} + \overset{\substack{\text{Glycerin}\\ \text{phosphoric acid.}}}{C^{8}H^{9}PO^{6}} + \overset{\text{Neurin.}}{C^{5}H^{15}NO^{2}}.$$

According to Diakonow, lecithin may exist in combination with each of the three fatty acids; as distearin-lecithin, dipalmitin-lecïthin and diolein-lecithin. He looks upon it as a salt of distearyl-glycerin phosphoric acid in combination with neurin as a base.*

Neurin or Cholin. In 1849† Strecker discovered in the bile of pigs a body which in 1862‡ he found also in ox bile. This body he named cholin; and it is prepared by the following method: Fresh ox bile is decomposed by boiling with baryta water; by this the greater part of the colouring matter, mucus, fat, and cholestearin is thrown down. To the filtered solution much hydrate of baryta is added, and the whole is boiled for about 12 hours. Sulphuric acid now throws down both the baryta and the cholalic acid, which may be separated from one another by means of boiling alcohol. The filtrate is now evaporated on a water bath, and so much sulphuric acid added as to drive out the hydrochloric acid completely. By treating the remainder with spirit, the sulphates remain behind with the taurin and a part of the sulphate of glycocoll. The alcoholic solution is evaporated so as to drive off the ammonia and is then boiled with hydrate of litharge. The filtrate is freed from lead by sulphuretted hydrogen and after evaporation and extraction with alcohol, the solution is decomposed with a little hydrochloric acid and chloride of platinum: there is thrown down a precipitate of a body formed by cholin in combination with chloride of platinum.

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* Diakonow, Hoppe-Seyler's *Med.-Chem. Untersuchungen*, Berlin, 1866-71, pp. 221 and 403.

† Strecker, *Annalen d. Chemie u. Pharm.* 1849, Bd. lxx. p 196.

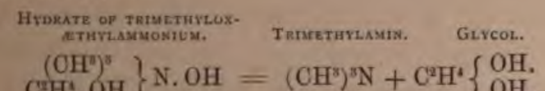
‡ Idem, *ibid.* 1862, Bd. cxxiii. p. 353.

The formula for this is $C^5H^{15}NO,\ HCl + PtCl^2$. Cholin when free would be an ammonia base whose formula would be $C^5H^{13}NO$. The rational formula is unknown; but it may be an amylenoxyd-ammonia, $C^5H^{10}O,\ NH^3$; or an æthyloxyd-trimethylamin $C^2H^4O\ C^3H^9N$.

Cholin is with difficulty soluble in absolute alcohol, but readily in dilute. Strecker has obtained cholin in combination with carbonic, sulphuric, nitric, and oxalic, acids.

Both Dybkowsky[*] and Baeyer[†] believe that Strecker's cholin is identical with the body which O. Liebreich has obtained from brain substance and which he calls neurin.[‡]

According to Würtz, neurin is hydrate of trimethyloxæthylammonium[§] which is changed by heat into trimethylamin-glycol.



HYDRATE OF TRIMETHYLOXÆTHYLAMMONIUM. TRIMETHYLAMIN. GLYCOL.

$$\left.\begin{matrix}(CH^3)^3\\ C^2H^4.\,OH\end{matrix}\right\}N.\,OH = (CH^3)^3N + C^2H^4\left\{\begin{matrix}OH.\\ OH.\end{matrix}\right.$$

It would seem probable that it is the lecithin in the bile which is the source of the neurin; for lecithin easily breaks up, and one of the products of its decomposition is neurin. Trifanovsky, however, takes another view, and believes that the neurin exists in the bile in some combination with either the biliary or the fatty acids.* Both of these opinions are of course pure hypotheses.

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[*] Dybkowsky, *Journal f. prak. Chemie*, 1867, Bd. c. p. 153.

[†] Baeyer, *Annal. d. Chemie und Pharm.* 1866, Bd. cxxl. p. 306.

[‡] O. Liebreich, *ibid.* 1865, Bd. cxxxiv. p. 29.

[§] Würtz, *Journal f. prakt. Chemie*, 1868, Bd. cv. p. 411.

Organic Salts. Some soaps, salts of the fatty acids, palmitate, stearate, and oleate of soda are found in the bile. The salts of these acids were noticed to be present in the bile by Tiedemann and Gmelin.†

Dogiel has noticed the presence of acetic and propionic acid in the fresh bile of oxen. The bile was decomposed by boiling with baryta, the baryta and cholalic acid thrown down by sulphuric acid, and the filtrate distilled. An acid fluid, smelling of butyric acid, came over. This product of distillation was neutralised by baryta, the baryta in excess removed by carbonic acid, and the fluid evaporated to crystallization. Acetate and propionate of baryta were formed.‡ It would seem quite possible that the presence of acetic and propionic acids in the bile may be products of decomposition, due to the process employed.

Urea. Popp finds urea a constant constituent of the bile of oxen and pigs. His method is to dilute the bile taken from the gall bladder immediately after death, and then to precipitate with lead, to remove superfluous lead with sulpheretted hydrogen, and then to evaporate the filtrate to dryness on a water bath. The residue consists chiefly of acetate of soda and urea.§ Jacobsen, however, found no urea in human bile freshly gathered from a biliary fistula; in one specimen a trace of leucin was found, but no tyrosin.‖

Leucin. Berlin found, in the gall bladder of a *Sarcoramphus papa*, a kind of vulture, crystals which, from their shape seen under the microscope, he judged to be formed of leucin.* As, however, no chemical tests were used for the further identification of the body, much stress must not be laid on the observation. The ova of nematoids were found in the mucus of the bile.

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* Trifanovsky, *Arch. f. d. ges. Phys.* 1874. Bd. ix. p. 497.

† Tiedemann and Gmelin, *Recherches* &c. *sur la Digestion*, Paris, 1826. Ière partie, p. 89.

‡ Dogiel, *Journal f. prak. Chemie*, 1867, Bd. ci. p. 298.

§ Popp, *Annalen d. Chemie u. Pharmacie*, 1870, Bd. clvi. p. 88.

‖ Jacobsen, reported by Westphalen, *Deutsches Arch. f. klin. Med.* 1873. Bd. xi. p. 603.

Sugar. A saccharine body is said by some writers to have been found in the bile by Macbride.† And after the discovery of the sugar-making function of the liver by Claude Bernard, sugar itself was found in the bile. But this is a purely *post-mortem* phænomenon, for if the bile be examined immediately after death, no sugar can be found. The appearance of sugar in the bile is due to endosmosis from the liver itself.‡ This applies only to health.

Albumen is not found in the bile, at least in health. It is not uncommon to find it in the bile of the human gall bladder; but, as in the case of sugar, it is most commonly a *post-mortem* appearance. A very slight trace of some albuminous body was found in the two first specimens of fresh human bile examined by Jacobsen, but it is doubtful if they were not impurities.§ In former times, the mucus which is found in cystic bile in large amount was taken for albumen.‖

Inorganic Salts. There is nothing peculiar about the alkaline salts of the bile. Their base is chiefly soda, the chloride being in large quantity, then phosphate and carbonate; there are also present phosphate of lime and chloride of potassium: small quantities also of magnesia and silica have been found.

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* Berlin, *Arch. f. d. holländischen Beiträge zur Natur- und Heilkunde*, Utrecht, 1858, Bd. i. p. 103.

† See Platner, *Ueber die Natur und den Nutzen der Galle*, Heidelberg, 1845, p. 1. I have, however, looked through David Macbride's *Experimental Essays on Medical and Philosophical Subjects*, Second edit. Lond. 1767, especially the essay on fixed air, but I have not found the statement that bile contains sugar.

‡ Claude Bernard, *Leçons sur les propriétés physiologiques et les altérations pathologiques des liquides de l'organisme*, Paris, 1859, t. ii. p. 207.

§ Jacobsen, *loc. cit.*

‖ Thenard, *Mémoires de Physique et de Chemie de la Société d'Arcueil*, 1807, t. i. p. 56.

The presence of iron has been noted in the bile from the days of Cadet* down to the latest researches of the last year or two.† It appears to be in exceedingly small quantity; not more than a milligramme in 20 C.C.‡

Copper also would appear to be a constant constituent of the bile, in very small traces. It seems to have been first found by von Gorup-Besanez§ in the bile, a year after copper had been found in gall stones by Bertozzi.‖

Gases. The gases of the bile have been studied by Pflüger, but only in two instances. The gall bladder of a freshly killed dog was opened under mercury, and the gases estimated. In the first experiment the following was the result:

Oxygen	·2 *per cent.*
Carbonic acid, driven out by phosphoric acid .	41·7 „
Carbonic acid, pumped out	14·4 „
Nitrogen	·4 „

In the second experiment the result was different:

Oxygen	*none*
Carbonic acid, driven out by phosphoric acid .	·6 *per cent.*
Carbonic acid, pumped out	5· „
Nitrogen	·6 „

The amount of bile used in the experiments was very small, and a large error may thus have crept into the figures.¶

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* Cadet, *Mémoires de l'Académie royale des Sciences*, Année 1767. Paris, 1770, p. 483.

† Kunkel, *Arch.f.d.ges. Phys.* 1877. Bd. xiv. p. 353.

‡ Marcet found in a man who had made a practice of swallowing clasp knives ·5 grain of prussian blue in 150 grains of bile; while in 150 grains of ordinary bile only ·2 grain were found. (*Med. Chir. Trans.* 1823, vol. xii. p. 63.)

§ F. von Gorup-Besanez, Heller's *Arch. f. phys. und path. Chemie*, 1846. Jahrg. iii. p. 17.

‖ Bertozzi, *ibid.* 1845, p. 225, (wrongly paged 522), from Polli's *Annali di Chimica*, Milan, 1845, p. 32.

¶ Pflüger, *Arch.f. d. ges. Phys.* 1869. Bd. ii. p. 173.

A few months after Pflüger, Bogoljubow published a series of estimations of the carbonic acid contained in the bile of dogs, and, in one case, of a sheep. In the first analysis the bile was freshly secreted and taken at once from the hepatic duct.

Carbonic Acid in 100 C.C.

	Uncombined.	Combined.	Total.
1.	19·5	37·	56·5
2.	17·1	62·5	79·6
3.		25·4	
4.	12·3		
5.	10·5	2·4	12·9
6.	6·8		
7.	5·06		
8.			12·1
9.	3·16	·29	3·45
10.	15·6	·6	16·2

This last was from the bile of a sheep.

The amount of carbonic acid in the bile is especially noteworthy, and would seem to show that some is made in the liver, as the amount is greater than in other secretions. Bogoljubow seems to think that the freshly secreted bile holds much more carbonic acid than bile which has been a long time in the gall bladder: and that the longer the bile has been in the gall bladder the less carbonic acid it holds.*

Noel found in the bile of a dog:†

Oxygen	1·22 *per cent.*
Carbonic Acid . . .	4·63 „
Nitrogen	9·13 „

Hoppe-Seyler finds that the bile taken freshly from the liver during digestion either contains no absorbed oxygen, or that it holds less than ·5 *per cent.* of this gas.‡

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* Bogoljubow, *Centralblatt f.d. med. Wiss.* 1869, p. 657.

† G. Noel, *Étude générale sur les variations physiol. des gaz du sang*, Thèse de Paris, 1876. Quoted by Hoppe-Seyler.

‡ Hoppe-Seyler, *Phys. Chemie*, Berlin, 1878, p. 307.

CHAPTER IV.

PHYSICAL AND CHEMICAL APPEARANCES OF THE HUMAN BILE.

The appearances of bile seen under the microscope are unimportant and in no way comparable to those of the urine, the organic and inorganic sediments of which give to the physician such valuable information. The first person who studied the bile with the aid of the microscope appears to have been Achilles Mieg, who, in a letter to Haller, says that he found nothing particular in some ox-bile that he had looked at save round shining drops, marked at their edges, which he compares to those seen in dried gum.[*]

Delius not only described the appearances seen under the miscroscope in bile but also had them engraved. He has indeed left an almost exhaustive account of what little there is to be noted. He speaks first of certain cubical crystals from human bile which, from their pointed ends as seen in the plate, and the arrangement of their square surfaces together, might be set down as cylindrical epithelium. In ox gall he saw but few of these square crystals, but abundance of granules arranged in stellate lines. In a capon he found rounded figures, in the plate they look like oil drops, which Delius says were of a violet or blue colour. In the bile of fish he found again cubical bodies or parallelopipeds.[†]

Weber noted also certain round and elliptical globules, of different sizes, in general small; and smaller than those seen in the milk and mucus.[*] Ducrotay de Blainville speaks of granules like fat, spots of colouring matter, and occasionally vibriones.[†] These vibriones were never seen by Bouisson in his observations,[‡] although they were detected by Charcot and Gombault in the cystic bile of certain animals whose bile ducts had been ligatured.[§] Bouisson says that the bile when seen under the microscope usually presents only a yellow layer; sometimes a few mucus globules and tables of cholestearin. Much the same remark is made by Fauconneau-Dufresne and Mandl.[||]

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[*] Achilles Mieg, *Epistol. ab eruditis viris ad Albert. Haller script.* pars iv. Bernæ, 1774, vol. iv. p. 104.

[†] Henrici Friderici Delii *super bile humana observationes nonnullæ microscopico chemicæ* Epistola ad Gulielmum Michaelum Richterum, Erlangæ, 1788. It is contained in Richter's *Circa bilis naturam*, Erlangæ, 1788, p. xliv.

Frerichs describes the following bodies as seen under the miscroscope: (i.) rounded balls, transparent or greyish, usually grouped together and removed by alcohol and acetic acid, but not by filtration. (ii.) Conical yellow bodies joined together in rows, without any nucleus that could be made out. (iii.) Certain bodies not peculiar to the bile, to wit, black or dark brown granules, which disappear on the addition of caustic potash; apparently pigment granules. (iv.) Rarely small crystals in colourless rhombic tables of cholestearin.[¶]

In Gorup-Besanez' description of the bile seen under the miscroscope, he divides the appearances into two heads; those constant, and those variable.

There are two constant appearances: (i.) molecular granules, very like coagulated albumen, only yellow or yellow brown, and refracting the light strongly. He thinks these are only coagulated mucus. (ii.) Epithelium of the gall bladder and ducts.

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[*] Weber, *Anatomie des Menschen*, Bd. i. p. 163. quoted by Burdach, *Traité de Physiologie*, Jourdan's ed. Paris, 1837, t. vii. p. 440.

[†] Ducrotay de Blainville, *Cours de phys. gén. et comp.* Paris, 1829, t. iii. p. 140.

[‡] Bouisson, *De la bile*, Montpellier, 1843, p. 23.

[§] Charcot and Gombault, *Archives de Physiologie*, 1876, p. 289.

[||] Fauconneau-Dufresne, *Traité de l'affection calculeuse du foie*, Paris, 1851. p. 39.

[¶] Frerichs, *Archiv. f. phys. u. path. Chemie*, 1845. p. 442.

The variable appearances are: (i.) Cholestearin: in 100 cases, the rhombic tables peculiar to this body were only seen three times; in the bile of cases of chronic Bright's disease, wasting after typhoid, and hypertrophy of the heart. In the last case, the bile deposited an abundant sediment of shining particles, and 20 gall stones were already present in the gall bladder. (ii.) Crystals of margarin. (iii.) Drops of fat. (iv.) Taurin. (v.) Blood; the bile must be concentrated to show the corpuscles: if thin, it dissolves them and it is to this that the solution of the corpuscles by the bile is to be attributed. (vi.) Pus corpuscles.[*]

E. Neumann has found in the bile of a man, who died of pneumonia, bodies exceedingly like the *corpora amylacea* of the prostate. They were, however, much smaller; the largest had only a diameter of 0·028 mm. and the great number were not nearly so large. In form, they were some circular, others oval, or of no regular shape, but showing a three or four-pointed figure with angles rounded off. They all showed distinctly concentric rings. In the centre of most was a small cavity from which rents spread out towards the circumference. These bodies had a fatty look, and were coloured yellow, apparently from the bile. Iodine coloured them green, which was changed into a bluish green by dilute sulphuric acid. In the gall bladder there was a large quantity of gall stones.[†]

The temperature of the bile at the moment of its secretion is unknown.

Some observations on the electricity of the bile were made by Bellingeri, but they are of no value in the present state of knowledge.[‡]

It cannot be said that our knowledge of the properties of human bile is in a satisfactory state. The earlier observations both on men and brutes, were all made on bile taken from the gall bladder after death, or as soon as the beasts were slaughtered. Bile, however, which has made a long sojourn in the gall bladder may be looked upon as dead bile.[*] It contains a far larger amount of solid matter, much mucus, and has lost the property of changing starch into sugar. It is only quite lately that an attempt has been made to study more closely the properties of active bile, freshly secreted by the liver. This has again and again been done in animals since the method of making biliary fistulæ has been found out, but in man very few opportinuties have offered themselves for any prolonged investigation of this sort; biliary fistulæ, formed by disease or injury, being very rare; and in the few cases known it is only in two, and and these published within the last ten years, that any accurate observations have been made.[†]

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[*] Von Gorup-Besanez, *Untersuchungen über Galle*, Erlangen, 1846. p. 28, and Heller's *Archiv. f. phys. u. path. Chemie u. Microscopie*, 1846. Jahrg. iii. p. 1.

[†] E. Neumann, *Arch. f. mikros. Anatomie*, 1866, Bd. ii. p. 510.

[‡] Bellingeri, *Memorie della reale Accademia delle Scienze di Torino*, 1827. t. xxxi. p. 314.

The two cases to which I refer are reported by H. Westphalen[‡] and Johannes Ranke.[§] Westphalen's case is that of a man aged 32, who had an opening made in the fifth right intercostal space for an empyema. About 400 C.C. of stinking pus came out, followed some days later by bile. From May 16. to May 30. the fæces were colourless, and during this time the observations were made.

The case of Johannes Ranke was also seen in a man, aged 38, in whom there existed a communication between the bronchi and an echinococcus sac in the liver. The patient brought up a quantity of bile by the mouth, but it is a matter of necessity that the bile thus offered for examination should be impure; and the inferences, therefore, drawn from its examination are less trustworthy than those taken from a case in which the fistula opened directly upon the surface of the body.

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[*] Dr. Kemp (*Proc. of Royal Society*, 1856. Vol. viii. p. 133.) believes that the mucous membrane of the gall bladder, or the mucus secreted by it, decomposes hepatic bile.

[†] An early attempt at the examination of human bile is mentioned by Haller (*Elem. Phys.* Lugd. Batav. 1764, t. vi. p. 605.) "In homine cui latus apertum bilem ex vesicula emittebat, Cajetanus Tacconus cysticæ bilis solius 4. uncias vidit eodem tempore fluxisse."

[‡] H. Westphalen, *Deutches Arch. f. klin. Med.* 1873. Bd. xi. p. 588.

[§] Johannes Ranke, *Die Blutvertheilung u.s.w.* Leipzig 1871. p. 144.

In Westphalen's case it was found that freshly secreted bile was of bright golden yellow colour, and it was only by exposure to the air that it showed the well-known changes into brown and green. In other cases of biliary fistula, the colour has been said to be greenish yellow,[*] greenish,[†] grass green,[‡] or greenish brown.[§] The belief of the best physiologists, as expressed by Dr. Lauder Brunton,[‖] would seem to accord with the statement of Westphalen.

Westphalen and von Wittich both found the bile free from viscidity. Von Wittich examined two portions. The first was clear and limpid. The second not so clear; and after standing some hours showed a change in colour which passed into yellow brown, and at the same time a yellow precipitate was thrown down.

The highest specific gravity which Westphalen observed was 1016, the lowest 1008. The mean of 22 days' observation was 1010·4. Johannes Ranke's mean was 1025, but the sources of error in this case must not be forgotten.

The reaction was neutral or barely alkaline, according to Westphalen and Jacobsen. Von Wittich found it clearly alkaline, and the same observer has shown that fresh human bile contains a ferment which has the power of changing starch into sugar. This power does not appear to be enjoyed by bile taken after death from the gall-bladder.*

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[*] MacPherson, *American Journal of Med. Sci.* 1871. Vol. lxi. p. 409. Laboulbène, *Union méd.* 1875, t. xx. p. 273.

[†] Grandclaude, and Dassit, in Fanconneau-Defresne's *Traité de l'affection calculeuse du foie*, Paris, 1851. pp. 307. and 311.

[‡] John Harley, *Med. Chir. Trans.* 1866. Vol. xlix. p. 89.

[§] Von Wittich, *Arch. f. d. ges. Phys.* 1872. Bd. vi. p. 181. An account of this case has also been published by Hertz, *Berlin. klin. Woch.* 1873. p. 161.

[‖] Lauder Brunton, in Sanderson's *Handbook for the Physiological Laboratory*, Lond. 1873. p. 495.

In Johannes Ranke's case, the solids of the bile were found to vary from 2·69 *per cent.* to 4·01 *per cent.* In Westphalen's case the mean was 2·25 *per cent.* a much lower figure.†

In Johannes Ranke's case, the bile acids formed 40 to 78·8 *per cent.* of the total solids, the mean being 53·45 *per cent.* The fats with cholestearin from 4·8 to 22·5 *per cent.* the mean being 14.48 *per cent.* The pigments and mucus from 10·28 to 24·11 *per cent.* the mean being 17·29 *per cent.* The ash varied from 13·1 to 17·8, the mean being 14·79 *per cent.*

These figures are somewhat different from those given by Jacobsen, the chemist who analysed the bile of Westphalen's case. They are as follows:

Of the organic constituents, 3·14 *per cent.* of dry bile was soluble in anhydrous æther: of this were:

Cholestearin	2·49 *per cent.*
Fatty matters	·44 „
Lecithin	·21 „

The lecithin was estimated by the amount of phosphorus. The bodies insoluble in æther and alcohol, probably coloured mucin, made up 10 *per cent.* of the solids.

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* J. Jacobsen (quoted by von Wittich, *Arch. f. d ges. Phys.* 1872. Bd. vi. p. 182. from an inaugural Diss. *de sacchari formatione fermentoque, etc.* Regimont. 1865.) finds the same power in the fresh bile of frogs, pike, carp, sheep, calves, oxen, swine, rabbits, cats, horses, geese, ducks, and fowls. Only once, however, did he find it in human bile, apparently taken from the gall bladder after death.

† In the lower animals the amount of solids seems to vary much in different tribes. Thus Bidder and Schmidt found that the fresh secretion of the liver of cats, dogs, and sheep, gave an average of 5 *per cent.* of solids; of rabbits, hardly 2 *per cent.*; but of geese and crows 7 *per cent.* The contents of the gall bladder in cats, dogs, and rabbits gave 10 to 20 *per cent.* of solids; but of sheep not more than 8 *per cent.* In geese, the amount of solids was from 10 to 20 *per cent.*; in crows it was as high as 25 *per cent.* (Bidder and Schmidt, *Die Verdauungssäfte,* Mitau and Leipzig, 1852. p. 214.) The fresh bile of guinea pigs holds, according to Heidenhain, not more than 1·35 *per cent.* and does not give a reaction with Pettenkofer's test (*Arch. f. Anat. Phys.* u.s.w. 1860. p. 648.)

The alcoholic extract of dry bile contained:

Glycocholate of soda	44·8 *per cent.*
Palmitate and stearate of soda . .	6·4 ,,

that is 51·2 *per cent.* of dry bile.

Jacobsen gives the following table of the amount of the inorganic constituents:

	Per Cent. of Ashes.	Per Cent. of Dry Bile.	Per Cent. of Fluid Bile.
Chloride of potassium	3·39	1·276	0·029.
Chloride of sodium	65·16	24·508	0·557.
Carbonate of soda	11·11	4·180	0·095.
Phosphate of soda	15·90	5·984	0·136.
Phosphate of lime	4·44	1·672	·038.
	100·00	37·620	0·855.

The bile contained not a trace of sugar or of any other body which would reduce copper. Urea was not present. Only in the first tested specimens were traces of albuminous bodies and of leucin found, but no tyrosin was ever discovered. Quinine and mercury were also not found in the bile when they were looked for, apparently after being administered by the mouth.

Of the better known biliary pigments bilirubin and biliverdin were detected. Copper could always be found in traces in the ash of the bile.

By decomposing the soda salts, soluble in alcohol with hydrate of baryta, glycocoll only was formed, and not a trace of taurin. The absence of taurocholic acid could also be directly ascertained, as the dried bile was completely free from sulphur.

This statement is contrary to the common belief of physiologists. Taurocholic acid is said by Dr. Lauder Brunton to be the chief acid in human bile.*

Jacobsen later on found taurocholic acid in the bile from the gall bladders of persons dying of various diseases, in one case even as much as 14·2 *per cent.* of the dry bile. The bile also contained small quantities of iron, silica, magnesia, and a trace of copper.†

The bile taken after death from the gall bladder of healthy men killed by accident was examined years ago by Frerichs‡ and von Gorup-Besanez§ whose papers appeared almost at the same time. Analyses of the bile of persons dying of diseases not connected with the liver, have been more lately made by Trifanovsky|| and Socoloff.¶

Frerichs describes healthy bile from the gall bladder as always being of a full brown colour, in thin layers brownish yellow, never green. In old persons it is darker. Its consistence is watery and thin; only in the last drops, or in the bile of new born children is a viscid appearance seen: von Gorup-Besanez thinks that the colour of the healthy bile may pass through all shades of colour, from pale yellow to black; and that the consistence may be that of tar, or thin as water.

The specific gravity, according to Frerichs, was in three cases 1040; in one only 1032. Von Gorup-Besanez has made no observations himself on the specific gravity, but quotes John, Schübler, and Kapff as finding it 1026. Bouisson also gives the same figure.**

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* Lauder Brunton, *loc. cit.*

† Jacobsen, *Berichte d. deutschen chem. Gesellschaft*, 1873. Bd. vi. p. 1026.

‡ Frerichs, *Hannoversche Annalen*, 1845. Jahrg. v. p. 42. Also in Heller's *Archiv f. phys. und path. Chemie*, 1845. p. 442.

§ Von Gorup-Besanez, Heller's *Archiv f. phys. and path. Chem.* 1846. Jahrg. iii. p. 1. and *Untersuchungen über Galle*, Erlangen 1846.

|| Trifanovsky, *Arch. f. d. ges. Phys.* 1874. Bd. ix. p. 492.

¶ Socoloff, *ibid.* 1876. Bd. xii. p. 54.

** Bouisson, *de la Bile*, Montpellier. 1843. p. 13.

The smell of the bile is said by von Gorup-Besanez to be peculiar: disgusting, and like the smell of human fæces. In my own opinion this is by no means common, and the human bile has rather an aromatic smell. The taste is notoriously bitter. The reaction was found in von Gorup-Besanez'* two first cases to be neutral, and this appears to be the case more often than that the reaction is alkaline.

The results of Frerichs' analysis of the bile of two healthy young men in a percentage are as follows:

	AGED 18.	AGED 22.
Water	86·00	85·92.
Solids	14·00	14·08.
Soda salts of the bile acids .	7·022†	9·14.
Cholestearin	·16	·26.
Margarin and olein . . .	·32	·92.
Mucus	2·66	2·98.
Chloride of sodium . . .	·25	·2.
Phosphate of soda . . .	·2	·25.
Phosphate of lime and magnesia	·18	·28.
Sulphate of lime . . .	·02	·04.
Oxyde of iron	Traces	Traces.

Gorup-Besanez gives the following analyses:‡

	MAN AGED 49 BEHEADED.	WOMAN AGED 29 BEHEADED.	MAN AGED 68 DEATH BY ACCIDENT.	BOY AGED 12 DEATH FROM WOUND.
Water	822·7	898·1	908·7	828·1.
Solids.	177·3	101·9	91·3	171·9.
Bile Acid Salts . .	107·9	56·5		
Fats . . . . . . Cholestearin . .	47·3	30·9	73·7	148·0.
Mucus with Pigment	22·1	14·5	17.6	23·9.
Inorganic Salts . .	10·8	6·3		

In two fœtal twins of six months, Frerichs found the meconium, which he looks upon as little else but fœtal bile, to have the following composition when dried:

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* Von Gorup-Besanez, *Untersuchungen*, u.s.w. p. 44.

† In the original it stands 70·22. Clearly a printer's mistake.

‡ E. F. von Gorup-Besanez, *Lehrb. d. Chemie*, Braunschweig, 1862. Bd. iii. p. 469.

	I.	II.
Cholestearin, olein, and margarin	1·8	15·4.
Biliary resin (bile acids)	12·3	15·6.
Epithelium, mucus, pigment and salts	85·9	69·00.

Frerichs thinks the fœtal bile poor in biliary salts, but rich in carbon, as the liver is almost the only organ (?) by which carbon can escape during fœtal life.

Trifanovsky, under Hoppe-Seyler's direction, has made analyses of the bile taken after death from the human gall bladder. A quantity of bile, 529·611 grm. was collected from the bodies of those who died of any disease whatever; and a second quantity, 306·628 grm. from those whose livers were found free from disease. The bile was poured from the gall bladder into a vessel, filled with two thirds of alcohol, and so protected from decomposition. The results of the analysis are as follows:

	I.	Ash.	II.	Ash.
Water	90·878.		91·079.	
Solids	9·122.		8·921.	
A. Insoluble in spirit	2·808.		1·636.	
1. Soluble in water and acetic acid	0·134.	·082.	0·323.	·12.
2. Mucus and phosphate of iron	2·674.	·191.	1·311.	·013.
B. Insoluble in absolute alcohol	0·846.		1·82.	
1. Before precipitation with æther	0·76.	·442.	1·723.	·514.
2. After precipitation with æther	0·086.		0·097.	·06.
C. Soluble in absolute alcohol				
1. Taken up by æther	0·835.		1·023.	
a. Cholestearin	0·251.		0·335.	
b. Lecithin	0·524.		0·017.	
c. Fat			0·359.	
d. Soap	·06.		0·312.	
2. Precipitated by æther	4·633.		4·444.	

The precipitate thrown down by æther is commonly looked upon as made up of bile acids, though it certainly contains soap and alkaline salts. Trifanovsky divided it into several parts, and estimated in one the amount of sulphur, in the second the alkalies, in the third the chlorine, in the fourth the nitrogen, and lastly the amount of cholalic and fatty acids.

	1.	2.
Cholalic acid	49·753.	38·842.
Palmitic, stearic, and oleic acids .	15·095.	27·46.
Sodium as metal	3·619.	2·135.
Potassium as metal	1·106.	4·586.
Sulphur	·93.	2·5.
Chlorine	?	1·33.
Nitrogen	?	4·69.

But the total amount of these bodies, estimated separately, is considerably less than the amount given by the first analysis; so there must remain in solution in the æther some body which makes up the balance. And this is the case; it is a body rich in nitrogen, either ammonia or some organic base, not glycocholic or taurocholic acid. In reality, an organic base was procured in combination with chloride of platinum from the acid filtrate which was obtained by throwing down the cholalic acid with hydrochloric acid from its combination with baryta. From this filtrate there were obtained a few crystals of taurin and a little amorphous substance which still contained glycocoll. The combination with platinum, which was very soluble in water, showed crystals which suggested by their shape and colour some neurin compound; and this was verified by its amount of platinum; ·162 grm. of crystals gave ·052 grm. of platinum. A compound of platinum with neurin in purity would give ·0516 grm. of platinum.

It has been stated that neurin is present in human bile. According to Trifanovsky it does not arise from a decomposition of lecithin, but is more probably contained as some combination with the bile acids or some fatty acids.*

Socoloff, dissatisfied with all that had been done before him, determined to make a fresh analysis. He assumed that the bile was quite natural when taken after death from the bodies of persons whose disorder brought in its train no appreciable disease of the liver; an assumption which will not pass unchallenged. He made six analyses in the following manner: the bile was evaporated at a low temperature, and the solid matters extracted with absolute alcohol till the filtrate became quite colourless. This alcoholic extract was evaporated to a small amount, and then æther added until a precipitate were no longer thrown down. After two or three days the æther was poured off and the precipitate once more dissolved in alcohol, and thrown down with æther; and this procedure repeated so long as a precipitate could be seen and the æther remained colourless. In this way, bile acid salts with chloride of sodium and potassium are found in the precipitate with æther. Further, Socoloff estimated in these salts the amount of sulphur, after Liebig's method, by fusing with potash and nitre.

The mixture of alcohol and æther, containing the soaps, fats, cholestearin, and lecithin, was distilled, the residue dried at a low temperature and completely extracted with anhydrous æther. What was insoluble in æther was looked on as soap: what was soluble in anhydrous æther was held to be fat, cholestearin, and lecithin.

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* Trifanovsky, *Arch. f.d. ges. Phys.* 1874. Bd. ix. p. 492.

Age and Sex of Patient.	Middle Aged Man		Young Man.	Man aged 50.	Man about 50.	two Biles used.
Cause of Death.	Cerebral Hæmorrhage. Liver Hyperæmic.	Bright's Disease. No Disorder of Liver.	Phthisis, Liver Hyperæmic.	Heart Disease, Liver Hyperæmic.	Pleurisy and Emphysema, Liver Hyperæmic.	One of Phthisis, other of Heart Disease;
Solids insoluble in absolute alcohol. . . .	4·801	4·111	1·520	3·749	3·292	4·875.
Precipitate with æther, *i.e.* bile acids and chlorides of sodium and potassium	8·993	4·263	3·819	6·278	9·794	5·679.
Sulphur	·144	·071	·061	·089	·11	·081.
Taurocholic acid . . .	2·324	1·143	·928	1·449	1·782	1·317.
Taurocholate of soda. .	2·431	1·197	1·031	1·506	1·865	1·376.
Soap	1·524	2·082	1·303	1·320	1·046	1·442.

These figures represent the amount *per cent.* in fluid bile.

By this table it will be seen that human cystic bile suffers many variations in its quantitative composition. The precipitate with æther is that which is most variable; though the sulphur, and therefore the taurocholic acid, is most constant. Its mean was 23·833 *per cent.* of the precipitate with æther. The amount of soap was also nearly the same in all.* Ernst Bischoff and Lossen have made six estimations of the amount of sulphur in human bile, and they find the mean to be 1·5 *per cent.* The amount varied however from ·83 to 2·99 *per cent.* Like Socoloff, they find that glycocholic acid is the more abundant acid in human bile.† Külz, who employed a modification of Carius' method of estimating the sulphur, has in one analysis found only ·1358 *per cent.* of sulphur, an exceedingly low figure. Much the same amount was, however, found in the bile of sheep, pigs, calves, and oxen.‡

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* Socoloff, *Arch. f. d. ges. Phys.* 1876. Bd. xii. p. 54.

† Ernst Bischoff, *Zeitschrift f. rat. Med.* 1864. Bd. xxi. p. 147.

‡ Külz, *Arch. f. Anat. Phys.* u.s.w. 1872. p. 98.

To sum up, then, our present knowledge of the physical and chemical characters of human bile: The appearances seen under the microscope are unimportant; freshly secreted bile is a fluid, not viscid, of a golden yellow, brown, or green colour; its reaction is usually neutral, sometimes barely alkaline; its specific gravity about 1010. It contains about 2 to 3 *per cent.* of solid matter and has the power of changing starch into sugar. This power is lost if the bile remain long in the gall bladder; it then shows a deeper colour, is brown, and is of a higher specific gravity, 1030 to 1040, and becomes viscid from the presence of mucus. The amount of solids in this cystic bile varies from 8 to 17 *per cent.* but the relation of these solid constituents to one another does not seem to vary.

The soda salts of the bile acids make up about one half of the solid constituents; they may, however, vary from 40 to 70 *per cent.* of the solids. It is known that these bile acids are formed by a combination with glycocoll and taurin, but whether the cholalic acid of man be identical with the cholalic acid of the ox is not known. It is certain that a taurocholic acid exists in the bile of man, although now and then it may be entirely absent, the glycocholic acid being usually the dominating acid. This forms about three quarters of the soda salts of the bile acids, while taurocholic acid forms the remaining quarter.

It is known that bilirubin and biliverdin exist in human bile; the other bile pigments have not been found. Their amount has not been directly estimated. With mucus, it is thought to be from 10 to 15 *per cent.* of the solids.

The fatty matters, the cholestearin, the soaps, and lecithin, make up from 3 to 20 *per cent.* of the solids. They seem to vary inversely with the amount of inorganic salts. The salts may be from 15 to 35 *per cent.*

of the solid bile; and of these salts, about two thirds are made up of chloride of sodium. The remainder consists of phosphate of soda and lime, possibly a product of the lecithin, carbonate of soda, chloride of potassium, traces of magnesia and silica, and constantly traces of iron and copper.

Urea, sugar, leucin, tyrosin, and albumen are not found in health in human bile. Lecithin and neurin are found, but it is not known if the neurin exist in combination, or be a product of the decomposition of the lecithin.

The gases of human bile have not been examined.

As this page was passing through the press, I found that a research had been published quite lately as to the composition of the cholalic acid of human bile. Hammarsten of Upsala, asserts that human bile contains bilirubin and hydrobilirubin, and that the bile acid is chiefly a glycocholic acid; but the cholalic acid of this is quite different from the cholalic acid of oxen or swine. Bayer corroborates this statement, and gives $C^{18}H^{28}O^{4}$ as the formula of human cholalic acid.[*]

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[*] Hammarsten and Bayer, in Maly's *Jahresbericht ueber die Fortschritte d. Thierchemie f.* 1878. Bd. viii. p. 260. Wiesbaden, 1879.

CHAPTER V.

HISTORY OF THE PHYSIOLOGY OF THE BILE: THE SOURCES OF THE BILE IN THE ŒCONOMY.

IT would seem to us, who live in the present age, that the secretion of bile would be the first function of the liver to become known. We must, however, go back to the early records of medicine to see if this were really the case. And in few matters is it more clear that several hands had a share in the collection of books which we call Hippocrates than in the teaching about the humours of which the body is composed. The writer of the book *De Morbis Lib. i.* teaches that all diseases arise from two sources, bile or phlegm,[*] while the writer of *De natura hominis* insists that there are four humours, the blood, the phlegm, the yellow bile, and the black bile,[†] the proper balance of which in the body is health, disease arising when there is excess or defect of any of these humours. On the other hand, the writer of *De Morbis Lib. iv.* teaches also that there are four humours; but in his system the black bile is replaced by the dropsy, or water. (ὕδρωψ)[‡]

In the undoubted writings of Hippocrates there is but little information as to what is meant by bile.[*] It is a fluid, yellow and bitter,[†] formed from fat,[‡] seen indeed in the upper part of the digestive canal,[§] but also found in the head and chest.[||] It would seem doubtful if the yellow bile were anything more than some fluid or secretion that was yellow and bitter without any connexion with the liver; thus a yellow appearance of the back of the tongue, with a bitter taste, would be set down as a bilious disorder. And it is not till we come to *De Morbis Lib. iv.* that we find any suggestion as to the source of the bile. Speaking of the four humours which, it has been said, are, according to this writer, blood, phlegm, water, and bile, he says the blood is from the heart, the phlegm from the head, the water from the spleen, the bile from the spot which is upon the liver.[¶] Later on the same writer says: "Now I will speak of the bile, how and why it grows in the body, and how the part which is upon the liver draws it to itself. This is how it is: If a man have eaten or drunken something that is bitter, or perhaps bilious and light, and the bile becomes more abundant in the liver, forthwith the liver suffers, which the children call *cardia;* and we have seen, and it is plain to us that it comes from the food and drink: for the body draws to itself from the food all of the aforesaid humours: and the place which is on the liver draws to itself all that is bilious."[**]

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[*] *De Morbis*, Lib. j. cap. ij. and *De aff.* cap. i. Littré's ed. t. vj. pp. 143. and 208.

[†] *De nat. hom.* cap. iv. Littré's ed. t. vj. p. 39. The four humours followed the four seasons, and it is likely that they have some relation to the four elements. See Sir Thomas Browne on the number four (*Pseudodoxia Epidemica*, Bk. iv. chap. 12. Lond. sec ed. 1650. p. 178.)

[‡] Petersen (*Hippocratis nomine quae circumferuntur scripta ad temporum rationes disposita*, Hamburg, 1839, p. 37.) however, notes that Plato in the *Timæus*, one of his undoubted works, speaks of the four humours, while in other dialogues he speaks only of bile and phlegm.

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[*] It is plain that bile must have been talked about long before Hippocrates; the word χολή has cognates in the Sanscrit, Latin, Teutonic and Slav languages. The porta of the liver was also the part inspected in the sacrifices, so that it is likely that the gall bladder and its contents would early become known. The heart was inspected as well at a much later date.

[†] Hippocrates, *de veteri medicina*, cap. xix. Littré's ed. t. i. p. 619.

[‡] *Epidem.* Lib. vj, Sect. v. § 8. Littré's t. v. p. 319. See also Sect. vi. § 1. p. 323. Liebig revived the notion that bile was formed from fat (See *Animal Chemistry*, Lond. 1842. p. 148.)

[§] *De diaeta in acutis*, cap. 9. Littré's ed. t. ij. p. 295.

[||] *De diaeta in acutis*, cap. 11. Littré's ed. t. ij. p. 311.

[¶] *De Morbis*, Lib. iv. cap. 33. Littré's ed. t. vii. p. 544.

[**] *De Morbis*, Lib. iv. cap. 36. Littré's ed. t. vii. p. 550.

Aristotle, in his *History of Animals*, has noted, with considerable accuracy, the tribes in which the gall bladder is absent. Stags, he says, have no gall [bladder], but they have a colour in their tail which resembles gall; although their intestine is so bitter that dogs will not eat it, unless the stag be very fat. So also the livers of elephants are without gall [bladders]; yet if cut into, a bilious fluid will come out.[*]

In another place he says that the livers of those animals that have no gall [bladders] are well coloured and sweet. And of those that have gall, that part of the liver, which is under the gall, is most sweet. But those animals which have a liver not well tempered have also blood less pure; and hence the excrement which is called gall is secreted from them. And a little further on he says: Gall therefore is alone the excrement of the liver.[†]

The views of Galen are also very obscure as to the place where the bile is secreted. He reprobates the opinion of Asclepiades that the yellow bile was formed, not separated, in the bile passages,[‡] and speaks of the gall bladder as collecting the bile;[§] and that it receives the secretion, and casts it forth again.[‖] But in another passage he compares the functions of the spleen and the gall bladder in purifying the blood; the former purging it of the black bile; the latter of the bilious and serous humours.[¶]

Aretaeus seems to have taught that both the liver and the gall bladder were concerned in the secretion of bile: he says that if the liver be inflamed or scirrhous, but remain unchanged as to its function, then it begets (τίκτει) bile in the liver; and the bladder which is in the liver separates (διακρίνει) it,[*] but if the passages which convey the bile to the intestine be obstructed, then jaundice is caused. Here is more clearly expressed, of which one finds many traces elsewhere, the doctrine that in the liver the bile is formed, with the urine, black bile, and blood; but that the function of the gall bladder is to separate and collect the bile, just as the kidneys and spleen separate and collect the urine and black bile.

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[*] Aristotle, *History of Animals*, Book ii. chapt. xv. Taylor's trans. Lond. 1809, p. 58. Doves have no gall bladders; and it is from this fact that they are the emblems of guilelessness.

[†] Aristotle, *On the movement of animals*. Book iv. Chapter ii. Taylor's trans. p. 114.

[‡] Galen, *De nat. fac.* Lib. i. cap. xiii. Kühn's ed. vol. ii. p. 40.

[§] *De anat. admin.* Lib. vi. Cap. viii. Kühn's ed. vol. ii. p. 569.

[‖] *De nat. fac.* Lib. iii. cap. xiii. and *in Hipp. lib. de aliment. com.* Lib. iii. cap. xxiii. Kühn's ed. vol. ij. p. 187 and vol. xv. p. 352.

[¶] *De atra bile*, Cap. viii. Kühn's ed. vol. v. p. 140.

The teaching of Avicenna[†] would seem to be much the same as that of Aretaeus. He says that the blood is formed in the liver; and in it, the bile and black bile, and watery humour (*i.e.* the urine) are separated:[‡] and that the gall bladder draws to itself the subtle humour proper to it with the yellow bile.

Phineas Fletcher's *Purple Island* is a treatise in rhyme on the physiology of this little kingdom, man: and the opinions set forth in it may be taken as the popular belief in the days just before Harvey. In it the liver, not the gall bladder, is indicated as the seat of the secretion of the bile.[§]

Yet immediately after the Harveian Revolution, strange doctrines began to be taught as to the source of the bile. De Back, a physician of Rotterdam, set forth that the bile was not made by the liver, but by the coats of the gall bladder.* Sylvius propounded the same doctrine, but more at length: he says that the bile is formed from the blood brought by the cystic arteries to the gall bladder, and thence by the coats of the gall bladder it penetrates into the cavity. From the gall bladder it descends into the ducts; by the hepatic duct it ascends into the liver, and thence passes to the heart; by the common duct it passes into the intestine.†

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[*] Aretaeus, *On the causes and symptoms of chronic diseases*, Book i. chapter xv. Adams' ed. p. 324.

[†] Avicenna, *Opera*, Lib. iii. fen. 14. tract. i. *De anatomia hepatis*, Venetiis, 1608, Lib. i. p. 750. and p. 791.

[‡] I have read somewhere, I think in Daremberg's *Histoire des Sciences médicales*, that Albert and S. Thomas have strange views on the functions of the liver. It would be ill work looking into two such voluminous schoolmen without some guide; but I have found only two references to the word *jecur* in the ample index prefixed to the Venice ed. 1595 of S. Thomas; the views of Albert in the treatise *de somno et vigilia* (Tract ii. cap. iii. ed. Lugd. 1651. t. v. p. 75.) seem to be merely that the liver is the seat of the natural spirits, as the head is of the animal, and the heart of the vital.

[§] Phineas Fletcher, *Purple Island*, Canto iii. Cambridge, 1633. p. 29.

This doctrine of Sylvius was supported by Vieussens who says that he has demonstrated by experiment that the gall bladder is the only part of the body destined to separate the bile from the blood;‡ and according to Haller,§ the doctrine must have survived into the middle of the eighteenth century. Morgagni, too, considered it necessary to prove that obstruction of the cystic duct did not cause jaundice.||

Perverse as this teaching seems, there is yet something beyond it. G. E. Stahl says that there had been some who did not acknowledge that the bile was secreted by the body generally, and then at last excreted by the liver; but who had persuaded themselves that the bile was formed from the more subtle parts of the food, and ascended into the gall bladder through the

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* Jacobi de Back, *Diss. de corde*, Cap. vj. Lond. 1660. p. 379. The edition which I have seen is bound up and paged with Harvey's *Exercitationes*, Lond. 1661.

† Sylvius, *Praxeos Med.* Lib. i. cap. xliv. §§ ii. and iii. *Op. med.* Amstelod. 1679. p. 296. The Oxford editor of Nemesius, a Bishop of Emessa in the fourth century, says in his preface that the doctrine of Sylvius as well as that of the circulation of the blood was anticipated by Nemesius. I do not think that either claim holds good.

‡ Raymond Vieussens, *Traité nouveau des liqueurs du corps humain*, Toulouse, 1715. p. 355.

§ Haller, *Elem. Phys.* Lugd. Batav. 1764. t. vj. p. 587. I have not been able to see the authors whom Haller quotes.

|| Morgagni, *de sedibus* etc. Epist. xxxvii. § 10.

common duct.[*] I have not found this theory anywhere but in Stahl.

Malpighi did great service for the physiology of the liver and the bile; he pointed out that the liver was a conglomerate gland, made up of hexagonal or polygonal acini, not a mere mass of blood, as was once believed; that the bile duct was the excretory duct of the liver, as the ducts of the parotid, pancreas, &c. are to those glands; that the bile was made in the liver and passed into the intestines by the duct.[†]

For the last hundred years it has been the undisturbed belief of physiologists that the bile is excreted by the liver, and not by the gall bladder or ducts.

Source of the bile.—It was the opinion of Liebig that, in man and herbivorous animals, the bile was formed chiefly from the elements of the food which contain no nitrogen.[‡] It was thought that the formula of cholalic acid ($C^{24}H^{40}O^{5}$) showed its kindred to the fats. Redtenbacher found capric, caprylic, and valerianic acids amongst the products of decomposition of choloidic acid.[§] Von Gorup-Besanez thought choloidic acid and cholic, *i.e.* cholalic acid, but links in the chain of the decomposition of the fats:[‖] and it was a favourite theory, some five and thirty years ago, that the bile was derived chiefly from the decomposition of the fats; in fact, a return to a much older belief that the bile was a kind of soap.[¶] Lehmann noted that the portal vein held a large quantity of fat, which had disappeared in the blood of the hepatic vein, and he thought that this fat might serve in the secretion of bile.[*] Bidder and Schmidt, however, noticed that upon an exclusive diet of fat, the secretion of bile at once fell to the level of that in an animal from whom all food was withdrawn; so that they think that the nitrogenous elements of the food must be looked on as the chief source of the bile.[†] H. Nasse, in his earlier work, saw, however, a great increase of the secretion of bile, when with fat nitrogenous foods were also given.[‡] And a theory might be built upon these observations: the fats might be thought to furnish the cholalic acid, while the albuminous bodies, by their decomposition into taurin and glycocoll, gave these bodies to unite with the cholalic acid and thus form the conjugate acids. This theory is Küthe's;[§] and it is undoubtedly very plausible; but the facts on which it is founded hardly bear it out; Ritter, a pupil of Nasse, made observations on the results of a fatty diet, but did not obtain any striking results.[‖] No deductions can, in my opinion, be drawn from his figures: and, as far as I can make out, Nasse is the only observer who has noticed much increase of bile on mixed fatty and flesh diet.

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[*] G. E. Stahl, *Physiolog*. Sect. j. membr. vii. Arct. iv. De bilis secretione.

[†] Marcelli Malpighii, *De viscerum structurâ exercit. anat.* Londini, 1669. *De Hepate*, cap. vii. is a refutation of de Back and Sylvius.

[‡] Liebig, *Animal Chemistry*, Lond. 1842. p. 168.

[§] Redtenbacher, *Annalen d. Chemie und Pharm.* 1846. Bd. lvii. p. 166.

[‖] Gorup-Besanez, *ibid.* 1846. Bd. lix. p. 158.

[¶] It has already been noted (p. 74.) that Hippocrates thought bile was formed from the fat.

Frerichs suggested the idea that the bile might be formed from the starchy parts of the food;[¶] and Küthe also supports this notion by pointing out that if from four equivalents of starch, enough oxygen be taken, the formula of cholalic acid remains.[**]

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[*] Lehmann, *Physiological Chemistry*, Day's trans. vol. ij. p. 87.

[†] Bidder and Schmidt, *Die Verdauungssäfte und der Stoffwechsel*, Mitau and Leipzig, 1852. p. 236.

[‡] Nasse, *Commentatio de bilis quotidie a cane secreta copia et indole*, Marburg, 1851. p. 14.

[§] Küthe, *Zur Function der Leber*, in Heynsius' *Stud. d. phys. Inst. zu Amsterdam*, Leipzig and Heidelberg, 1861. p. 24.

[‖] Ritter, *Einige Versuche ueber die Absonderungs-Grösse der Galle von d. Nahrung*, Diss. Inaug. Marb. 1862. p. 33.

[¶] Frerichs, in Wagner's *Handwörterbuch d. Physiologie*, Braunschweig, 1846. Bd. iii. p. 831.

[**] Küthe, *op. cit.* p. 22.

4 eq. of starch $C^{24}H^{40}O^{20}$.
1 eq. of cholalic acid $C^{24}H^{40}O^{5}$.

Ritter, however, found that in a dog fed only on potatoes, or on potatoes and fat only, the amount of bile daily secreted fell very low.*

The amount of nitrogen in glycocoll, and of nitrogen and sulphur in taurin would certainly seem to point to an origin in the albuminous bodies of the blood or food.† Some part of these bodies is thought to be split up in the liver into taurin and glycocoll, while another part goes to form leucin, tyrosin, xanthin, and hypoxanthin, bodies containing nitrogen. Meissner would probably go a step further, and say that urea also was formed abundantly in the liver. Do the peptones at once furnish these nitrogenous bodies, or are they derived from the products of the decomposition of the tissues? Karl Voit would answer that the bile acids are derived, like urea, from the tissues,‡ while the great dependence of the bile-making functions upon the glycogenetic function would seem rather to suggest that they come immediately from the splitting up of the peptones.

Küthe has suggested an ingenious hypothesis as to the relations of the bile to the making of glycogen, which may be conveniently spoken of here. He found that when the bile is diverted from the intestine, no glycogen is formed in the liver; for example, when a biliary fistula is set up; or, as later experiments have shown, when the common duct is tied. Also in Moos' experiments of tying the portal vein, no bile and no sugar was found in the liver twenty-four hours after the operation. By tying the portal vein, the return of bile from the intestines to the liver by the blood would be stopped. Is it possible, then, that the circulation of the bile is needful for the making of glycogen? Küthe thought perhaps that the glycogen might take its source from the glycocoll and taurin of the conjugate acids. To prove this, food was withheld from a dog for 5 days, so that all the glycogen might disappear from the liver; then 5 grammes of glycocoll were given in water, and the dog was killed in 2½ hours. Sugar and glycogen were found in the liver. Also with taurin the like was seen. A dog was kept without food or drink for 8 days; and on the 9th day 4 grammes of taurin in water were given to him, and the dog was killed in 2½ hours. The liver held a good deal of glycogen and sugar, while sugar was present in the blood of the carotid.

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* Joseph Franz Ritter, *op. cit.* p. 32.

† See a paper by A. Froehde in Erlenmeyer's *Zeitschrift f. Chemie und Pharmacie*, 1864, Jahrg vij. p. 464.

‡ Karl Voit, *Phys.-Chem. Untersuchungen*, Augsburg, 1857. p. 41.

Küthe sets forth from this the following propositions: that the bile-making function is the chief function of the liver; and that the glycogenetic is subsidiary to the biliary function; *diabetes mellitus*, therefore, depends upon a greatly increased secretion of bile, while artificial diabetes depends upon an increased change of glycogen into sugar. At the same time that glycogen is formed, urea is formed also.*

Küthe's master, Professor Heynsius, says, on the contrary, that he does find glycogen in the livers of dogs in whom a biliary fistula has been set up. Out of three dogs, it was not present in one, but plainly present to the glacial acetic acid test in two others, while iodine gave a negative reaction in two, and a dubious reaction in the third. Heynsius, however, allows that diverting the bile from the intestine greatly decreases the amount of sugar in the liver. Heynsius also found that the length of time for which Küthe kept his dogs without food was not enough completely to free the liver from glycogen. Some small amount still remains at the end of a week's fast, and this amount was not increased by giving glycocoll or taurin to the animal shortly before death.*

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* Küthe, *passim*.

Mead (*A Mechanical Account of poisons*, Lond. 1747, 4th ed. p. 32.) says that diabetes is much akin to jaundice, and is a distemper, not of the kidneys, but of the liver, proceeding from a vitiated mixture of the bile.

If these experiments of Heynsius prove correct, it will undoubtedly cause Küthe's theory of the formation of glycogen solely from glycocoll and taurin to be abandoned. Not so, however, his views of the dependance of the bile and glycogen making functions of the liver upon each other. Bernard once thought them totally distinct† and was followed by writers who held that some cells of the liver secreted the one, and others the other. The two functions have undoubtedly a close relation to one another; for the ligature of the duct, or the diverting of the bile from the intestine, causes a great decrease of glycogen in the liver, if not an entire absence from that organ.

Secretion or only Excretion by the Liver.—In the seventeenth century, Glisson taught that the liver was a mere filter, by which the bile was strained off from the mass of the blood. The business of the liver, he says, is to take up by the porta the blood charged with bilious humours, to separate the bile, and then to return the blood made pure again into the cava.‡ This doctrine prevailed quite into our own times, and was specially favoured by physicians to whom it very conveniently furnished a theory of jaundice by suppression of secretion. After Budd, the doctrine was thought to be exploded, but it was revived by Liebermeister, who pointed out, quite truly, that the physiological demonstration of the secretion of the bile by the liver was wanting.*

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* Heynsius, *Die Quelle des Leberzuckers*, in *Stud. d. phys. Inst. zu Amsterdam*, Leipzig, and Heidelberg, 1861, p. 57.

† Claude Bernard, *Leçons sur les propriétés etc. des liquides de l'organisme*, Paris, 1859, t. ii. p. 203.

‡ Francisci Glissonii, *Anatomia Hepatis*, Cap. xli. Amstelaedami, 1659, p. 456.

The theory of the formation of the bile in the body at large was indeed thought to be disproved, specially by the experiments of Moleschott. He removed the whole of the liver from frogs; and found that in some cases the animals would live as long as three weeks: yet no trace of bile acids could be found in their blood, muscles, gastric juice, lymph, or urine.† Kunde preceded Moleschott in observations with the like object, but they are less valuable; Kunde's frogs survived at the most the fourth day.‡ Johannes Müller is commonly said also to have extirpated the livers of frogs; but, as his experiments are related by Kunde, he seems only to have thrown a ligature around the vessels of the liver, and afterwards to have found the same changes with nitric acid in the blood of healthy frogs as in the blood of those operated upon.‖

It may be objected to Moleschott's and Kunde's experiments, that they used chemical tests, not now very greatly trusted; for it is known that, in complex organic fluids like blood and urine, Pettenkofer's test may not at once detect the presence of bile acids. And a still further objection may be made; for when Leyden tied the bile duct only of frogs, no jaundice was seen at the end of 8 or 14 days. No trace of bile was found in the blood; and even in the liver not the least appearance of jaundice was seen.§ If no jaundice be caused by tying the duct, can any be looked for after removing the liver? The vital processes in these animals are very slow; and warm blooded animals do not survive the severe injuries inflicted by the removal of the liver.

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* Liebermeister, *Beiträge zur path. Anat. und Klinik d. Leberkrankheiten*, Tübingen, 1864, p. 241.

† Moleschott, *Arch. f. phys. Heilkunde*, 1852, p. 479.

‡ F. T. Kunde, *De hepatis ranarum exstirpatione*, Diss. Inaug. Berolin. 1850.

‖ Johannes Müller, quoted by Kunde, *op. cit.* p. 6.

§ Leyden, *Beiträge zur Path. des Icterus*, Berlin, 1866, p. 19.

Schmulewitsch, again, in Ludwig's laboratory, made some observations which seemed to show that the bile is really formed from the blood by the liver. He passed dog's blood whipped, and diluted with saline solution, through the portal vein of a recently-killed rabbit, and found that the secretion of bile went on, in a less degree than in health, for two hours and more, after death.[*] Pflüger, however, passed a 3 *per cent.* saline solution through the liver of a recently-drowned cat in whom the *rigor mortis* was just beginning to shew itself; he found an abundant secretion of a dilute bile to take place, and to last for more than an hour. This will show that the supposed secretion of the bile was only a transudation of serum into the fine biliary passages, and a pushing of the bile secreted before death into the large biliary ducts, giving rise to the factitious appearance of secretion.[†]

Röhrig has repeated both Schmulewitsch's and Pflüger's experiments, and decides in favour of the former. He finds that no bile makes its appearance when only saline solution is thrown into the liver; whereas abundance appears when the animal's own whipped blood is again and again passed through it.[‡]

In this state of affairs, where every experiment, which tends to shew that the liver itself secretes the bile, not merely separates it, is met with another to show that the first experiment does not answer its purpose, we shall be compelled to fall back on the general principles of physiology.

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[*] Schmulewitsch, *Arbeiten aus der phys. Anstalt zu Leipzig*, 1868, p. 113. M. Schiff says that in 1862 he made a similar experiment to that of Schmulewitsch; and after passing blood through the liver for a quarter of an hour about 17 centigrammes of freshly-secreted bile were collected (*Schweiz. Zeitschrift f. Med.* 1862. Bd 1. p. 50. quoted in *Arch. f. ges Phys.* 1870, Bd. iii. p. 610.)

[†] Pflüger, *Arch. f. d. ges. Phys.* 1871. Bd. iv. p. 54.

[‡] Röhrig, Stricker's *Med. Jahrbb.* Wien, 1873. p. 268.

blood in health, equal say to the cholestearin, it would be impossible that they could escape detection. I think myself this reasoning is valid; for the case of the urine of jaundice in which for so long the bile acids lay undetected is not in point, as the bile acids could not be found at any time, while it is acknowledged that they can be found in the blood in cases of jaundice or artificial injection.

But there is yet another argument. It is said that the liver is able to draw to itself and forthwith excrete whatever bile pigments may be present in the blood. Schiff found, when bile is injected into the duodenal fistula of an animal, which has also a biliary fistula, that a great increase of the secretion of bile from the biliary fistula takes place in 12 or 15 minutes after the injection. And with animals in whom an amphibolous biliary fistula had been made, that is, a fistula in which the bile could be directed into the intestine, or to the outside of the body at pleasure, it was found that a much greater amount of bile was secreted after the bile was allowed to pass into the gut than after it had been led out of the body. Further, if the bile acids were injected into the veins, stomach, or duodenum, or under the skin, a great increase in the solids of the bile took place.* Prince Tarchanoff found that when hæmoglobin or bilirubin was injected into the veins of an animal with a permanent fistula, a great increase in the amount of pigment took place.† Huppert, however, found that when the bile acids are injected into the veins of an animal with a biliary fistula, only a fourth or a third appeared in the bile,‡ and Socoloff has repeated these experiments with the bile acids, and thinks the liver has little power of excreting them.* Röhrig also found that when a solution of glycocholate of soda is injected into the portal vein, the pulse becomes slow, just as if the salt had been injected into a systemic vein:† an appearance which would hardly be consistent with the view that the liver has great power of rapidly excreting the bile acids.

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* Schiff, *Arch. f. d. gesammte Physiologie*, 1870. Bd. iii. p. 598.

† Tarchanoff, *ibid*, 1874, Bd ix. p. 329.

‡ Huppert, *Arch. d. Heilkunde*, 1864, p. 244.

By these observations the conjecture of some physicians, such as Dr. George Budd,‡ Skoda,§ and Dr. George Harley,‖ that the bile pigments are formed in the blood, not in the liver; and that the bile acids only are formed in the liver, may be thought to be favoured. It is of course possible that the hepatic cells may, as Dr. Michael Foster says,¶ avail themselves of certain half-made materials, such as hæmoglobin, the transference of which into pigment would be easy in the opinion of many physiological chemists. From Schiff's and Tarchanoff's experiments it is argued that the liver so rapidly excretes the bile pigments, that it at once gets rid of all contained in the blood or which are formed there; so that in health no bile-pigment can be detected in the blood. I must own that these excretions must be rapid indeed: more rapid than any other excretion that is known.

What vessel furnishes the elements of the bile? It has been much disputed whether the portal vein or the hepatic artery supply to the liver the materials out of which the bile is formed. The strife, which Dr. Michael Foster thinks is over a barren problem,** has been prolonged by the observations and experiments which are brought forward, and which tend to show, on the one side, that the blood of the portal vein is not necessary to the secretion of bile, and on the other, that it is.

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* Socoloff, *Arch. f. d. ges. Phys.* 1875, Bd. xi. p. 166.

† Röhrig, *Arch. d. Heilkunde*, 1863, p. 412.

‡ Budd, *On Diseases of the Liver*, Lond. 1857, p. 467.

§ Skoda, *Deutsche Klinik*, 1859, p. 286.

‖ George Harley, *Jaundice*, Lond. 1863, p. 11.

¶ Michael Foster, *Text-book of Physiology*, London, 1877, p. 191.

** Michael Foster, *loc. cit.*

These experiments go back as far as the days of Malpighi, who speaks of ligature of the hepatic artery close to the cœliac trunk as an often-repeated experiment: after the ligature a large amount of dilute bile was secreted.[*]

Abernethy noted in a well-nourished child, of about 10 months, brought to St. Bartholomew's Hospital for dissection, that the portal vein terminated in the *vena cava inferior*, nearly on a line with the renal veins. The gall-bladder contained a teaspoonful of bile, bitter to the taste, which became green when dilute nitrous acid was added.[†] Abernethy was evidently inclined to the belief that the blood of the portal vein was not necessary for the formation of bile.

Under the two heads of obstruction of the portal vein and obstruction of the hepatic artery, the different observations and experiments may be arranged.

i. *Obstruction of the portal vein.* When the portal vein of a mammal is suddenly tied, the animal dies within 24 hours at least of the operation: the greater number die immediately. In four rabbits who survived the operation about 24 hours, Moos found an absence of bile and sugar in the liver. In frogs, who live much longer, he found the secretion decreased during the first few days after the operation; while if the animal lived long, say four weeks, the bile was apparently increased in amount.[*] Oré discovered a plan by means of which a gradual obliteration of the portal vein took place. In all his dogs he found the gall-bladder full of bile.[†] It would, however, have been more conclusive, as Bernard remarks, if a biliary fistula had been established at the same time that the portal vein was tied,[‡] as the gall-bladder may have been filled by bile secreted before the operation. In disease it is not very uncommon to find a complete obliteration of the portal vein by clots, and in these cases the gall-bladder is often full. This of course affords as much or as little proof as Oré's experiments.

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[*] Malpighi, *Opera*, London, 1686. De Liene, p. 120 in the *De viscerum Structura.* Benjamin Phillips says that he tied both portal vein and hepatic artery, but noticed only a decrease of the secretion of bile. (*Lond. Med. Gaz.* 1833, vol. xii. p. 423.) Simon of Metz is said to have done the same. (*Journal de Progrès*, 1828, t. vii. p. 215.) I have not verified this last statement.

[†] Abernethy, *Phil. Trans.* 1793, Part i. p. 61. It is just mentioned by Lawrence (*Med. Chir. Trans.* 1814, Vol. v. p. 174) that a teacher of anatomy in London had met with a like state in the body of a much older person. Benjamin Phillips (*Lond. Med. Gaz.* 1833, Vol. xij. p. 423) gives two other cases; one by Lieutaud, (*Historia Anat.-Med.* Paris, 1767, t. j. p. 190) but this is a case of absence of the liver and spleen; and another by J. J. Huber, (*Observ. aliqu. Anat.* Casselis, 1760, p. 34) in which the portal vein is said to have passed through the diaphragm, *e ramis suis hepaticis mox productus*, but nothing is said of the bile.

Schiff, in some of his experiments on the influence of the circulation in the liver on the secretion of bile, tied all the structures in the hepato-duodenal ligament, save the hepatic artery. Occasionally, however, he tied the vessels separately; the bile was received by means of a cannula tied in the common duct. In cats, the ligature was followed by death in 40 to 90 minutes, no bile being secreted. The creatures rapidly became torpid, and artificial warmth in no way lessened this state. No rabbit survived the operation longer than 54 minutes. According to Schiff, the cause of death seemed to be the accumulation in the in the blood of the materials which ought to be excreted by the bile.

In dogs and cats, Schiff tied the portal vein after Oré's method, somewhat modified. In these creatures he found that the portal vein above the place of ligature made anastomoses for itself with the general systemic veins: in cats especially it was seen that a large branch from the umbilicus passed by the side of the *ligamentum teres* of the liver into the portal vein. To this vein Schiff gives the name of *vena parumbilicalis.* These observations do not, in Schiff's opinion, contradict the general belief that the bile is made by the portal blood. He made also an attempt to turn the blood from the renal artery into the portal vein, but the experiments did not succeed on account of the clotting of the blood in the vessels. The experiments on three animals lasted but a quarter of an hour, during which time the liver showed a dark red colour, but the secretion of bile went on.*

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[*] Moos, *Untersuchungen u. Beobachtungen ueber den Einfluss d. Pfortaderentzündung auf die Bildung der Galle und des Zuckers in der Leber*, Leipzig and Heidelberg, 1859. pp. 17 and 24.

[†] Oré, *Comptes rendus*, 1856, t. xliii. p. 463.

[‡] Claude Bernard, *Leçons sur les propriétés, &c. des liquides de l'organisme*, Paris, 1859, t. ij. p. 195.

In another set of experiments, Schiff intended to throw light on the absorption of bile by the portal system; he found that the amount of bile passed out of a biliary fistula in a dog whose portal vein was tied, after the injection of bile into the intestines, was no less than in one whose portal vein was free, so that the bile was absorbed from the intestines, carried into the general circulation and yet was at once discharged by the liver. It is a pity, however, that Schiff did not ascertain that no immediate communication in this dog between the intestinal vessels and the upper part of the portal vein had been set up.†

Röhrig found that if the vessels in the hepato-duodenal ligament were firmly compressed, the biliary secretion was at once arrested. If the compression did not last more than a few minutes, the liver slowly recovered itself. If it lasted longer, the animals died without another drop of bile being secreted. If the portal vein alone were compressed, there was a considerable decrease of the secretion of bile, but no such complete cessation, as there was after pressure on both vessels.[*]

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* Schiff, Canstatt's *Jahresbericht f.* 1862, Bd. i. p. 127.

† Schiff, *Arch. f. d. ges. Phys.* 1870, Bd. iii. p. 608.

ii. *Ligature of the hepatic artery.* It has been already said that Malpighi noted a flow of dilute bile after ligature of the hepatic artery. Brachet and Fouilhoux say that they attempted to tie the portal vein or the hepatic artery in living animals. The ligature of the artery appeared to them to suspend the secretion of bile, but not the ligature of the portal vein. They are cautious enough, however, to add that they draw no conclusions from these appearances, as the animals did not live long enough.[†]

Kottmeier[‡] and Küthe[§] found that no bile was secreted after ligature of the hepatic artery of rabbits, while Röhrig found but a slight decrease in the amount of bile secreted after the ligature of the hepatic artery;[‖] in what animal does not appear.

Schiff found that the ligature of the hepatic artery, behind the stomach of a large dog, was no hindrance to the secretion of bile. In fact the vessel never became empty of blood. He found in many dogs, that the ligature of the hepatic artery neither caused a stoppage of the arterial supply of blood to the liver nor of the secretion of bile. In both dogs and cats there are branches to the liver from the phrenic arteries, from the left coronary arteries of the stomach and from a small branch accompanying the bile ducts: so that it is necessary, to cut off all supply of arterial blood from the liver, that the three branches of the cœliac trunk and the phrenic arteries should be tied.[*] In case of ligature of the portal vein Schiff noticed no enlargement of the hepatic artery. Cohnheim and Litten confirm the statement that the arterial blood cannot be cut off from the liver by ligature of the hepatic artery in dogs. They find, however, that in rabbits this operation is possible, but is rapidly followed by death within the first 20 hours. A change in the liver takes place which Cohnheim and Litten call necrosis. On section the liver is seen to be soft, the colour grey yellow, not a trace of polish on the surface, the acini invisible: under the microscope the the section is seen clouded and indistinct, and in some cases the nuclei not discernible with the help of logwood.[†] These observations show the important influence which the hepatic artery has upon the nutrition of the liver; but they are not much aid in determining the question if arterial or portal venous blood be essential to the secretion of bile.

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[*] Röhrig, Stricker's *Med. Jahrbb.* 1873, p. 242.

[†] Brachet and Fouilhoux, quoted by Raikem, *Observations, etc. sur quelques affections morbides de la veine porte*, in the *Mémoires de l'Académie royale de Médecine de Belgique*, 1849, p. 15.

[‡] Kottmeier, *Zur Kenntniss der Leber*, Diss. Inaug. Würzburg, 1857, p. 11. Some experiments were made on frogs. In rabbits the gall bladder was found empty, and no bile in the intestines. See Cohnheim and Litten's observations on the next page.

[§] Küthe, *Studien des phys. Instituts zu Amsterdam*, herausgegeben von Heynsius, Leipzig and Heidelberg, 1861, p. 35. No glycogen or sugar was found in the liver of rabbits.

[‖] Röhrig, *loc. cit.*

Obstruction of the hepatic artery in disease is a rare phænomenon, much rarer than portal obstruction. Ledieu has recorded a case of aneurysm of the hepatic artery in which that vessel was obstructed, and yet the gall-bladder was full of bile.[‡] As the observations of Schiff teach, it is very hard to keep arterial blood out of the liver; in Ledieu's case the pyloric artery was pervious; and as this artery inosculates freely with the coronary artery of the stomach, there is no proof that the liver was deprived of arterial blood.

Reviewing these various observations, it will be at once seen that any deduction from supposed obstructions of the hepatic artery in man is of no value, and the whole of these may be passed by in silence. Whether the same objection will apply to obstruction of the portal vein, that is to say, whether the portal or other blood again finds its way to the liver in all cases, is not so certain. That the portal blood in many cases does not enter the liver, but the general circulation, would seem to be shown by Bernard's observation ; the blood of the portal vein was found anastomosing with the renal vein, and the *vena cava inferior*, thus reproducing in mammals the venous system of Jacobson.* Other anastomoses have been described with the intestinal and external systems.

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[*] Schiff, Canstatt's *Jahresbericht f.* 1862, Bd. i. p. 126.

[†] Cohnheim and Litten, *Arch. f. path. Anat.* 1876, Bd. lxvii. p. 162.

[‡] Ledieu, *Journal de Bordeaux*, 1856, Mars. reported in Schmidt's *Jahrbb.* 1857, Bd xciii. p. 56.

The earlier observations of the passage of the portal vein direct into the *vena cava* cannot be made of any service, as the sources of blood to the liver, other than the portal vein, are not spoken of.

The cases of sudden ligature of the portal vein which Moos records, would doubtless be set aside by many physiologists: yet it is noteworthy that 24 hours after the ligature no bile or sugar could be found in the liver; an effect hardly to be sought in the operation itself. It may therefore be thought that the sudden removal of the portal blood, the hepatic artery being free, has some influence both on the bile and sugar-forming functions of the liver, and that the functions of the liver only continue to be properly performed when the blood brought by both sets of vessels reaches the lobules. The matter is, however, a very difficult problem ; and I would prefer, with Bichat,† to leave it to the decision of further researches.

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* Bernard, *op. cit.* pp. 190 and 195. He indeed tied the portal vein suddenly on a pigeon: yet the animal died the next day, in spite of the communications between the portal and inferior cava in these creatures.

† Bichat, *Anatomie générale*, Paris, 1801, t. ij. p. 458. It seems to have been the general belief in Bichat's time that the bile was secreted from the portal vein. He gives fully the reasons then prevalent for this belief. Some of them seem to us foolish enough, and he has an easy task to refute them. Cf. Haller, *Elem. Phys.* Lugd. Batav. 1764, t. vj. p. 597, and Tiedemann and Gmelin, *Recherches, etc. sur la Digestion*, Paris, 1827, Partie ii. p. 57.

CHAPTER VI.

THE AMOUNT OF BILE SECRETED IN HEALTH AND THE AGENTS WHICH AFFECT IT.

Amount of bile daily secreted in health.—Before the observation of biliary fistulæ in men or animals, it was impossible to do more than guess at the amount of bile secreted by the liver. Nevertheless Haller set down the amount of bile daily secreted as 24 ounces;* a figure which approaches some of the calculations made of late years. Other physiologists about the same time set the amount much lower; a few drachms, or an ounce or two.†

Later on, more extravagant views prevailed; the amount of bile secreted in the 24 hours was calculated from the quantity thought necessary to neutralise the acid chyme, and an ox was said to secrete the enormous quantity of thirty seven and a half pounds of bile in a day.‡ Liebig adopted this statement as it coincided with some of his views on the sources of the bile and its importance in the processes of respiration and of animal heat:§ indeed the estimation seems for a time to have been generally accepted.

The views of these writers are indeed entirely speculative; and are in no way founded on observation. According to Bidder and Schmidt,‖ Douglas, an American physician, was the first in this century to form any opinion based on the analogy of experiments on animals; and from these data he calculated that a healthy man excreted during the 24 hours 29 ounces of bile.

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* Haller, *Elem. Phys.* Lugd. Bat. 1764, t. vi. p. 606.

† Bianchi, *Historia Hepatica*, Genevae, 1725, t. i. p. 116.

‡ C. H. Schultz, *de alimentorum concoctione*, Berolini, 1834, p. 108, 42 *et seqq.* quoted by Bidder and Schmidt, *Die Verdauungssaefte*, Mitau and Leipzig, 1852, p. 117.

§ Liebig, *Animal Chemistry*, Lond. 1842, Gregory's translation, p. 64.

‖ Bidder and Schmidt, *loc. cit.* They quote from Tiedemann, *Physiologie der Verdauung*, Ulm, 1835, p. 268. The reference to Douglas' work is: Medical Repository by Mitchill, New York, 1817. I have not been able to see a volume of the New York *Medical Repository* for 1817.

Magendie says that in dogs the escape of bile and pancreatic juice takes place by intervals; about twice in a minute a drop of bile is seen to rise from the papilla, and this drop spreads itself uniformly over the parts around.[*] With these two observers physiology seems to have contented herself during the first half of this century.

When Schwann, therefore, invented his mode of making biliary fistulæ in animals,[†] there appeared good hope that the great darkness which shrouded all that pertained to the secretion of the bile might be chased away. An increase in knowledge has certainly taken place, but the new method of observation has hardly done all that might have been looked for from it at the first moment of its discovery. One important defect is that the bile is diverted from the intestine, out of the body entirely: a circumstance not without considerable influence upon the physiology of the secretion.[‡]

Before considering the information given by experiments, it will be well to consider the results of the observations made in man when disease or accident has formed a biliary fistula. There are very few in which any observations have been made, and still fewer in which accurate and careful investigations have been carried out: and the observations are open to all the objections made against biliary fistulæ in animals. Further, it may be said that the observations are altogether untrustworthy, and that they were made on persons, all of whom were weakened by long illnesses, and most of them by a suppuration; and that the results in no way represent the qualities of the secretion in health. Of course these objections must be weighed; but the results on man, even if exhausted by disease, should be compared with those attained by observation on healthy animals, as these are the only two paths of attaining knowledge open to us.

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[*] Magendie, *Précis élém. de phys.* Paris, 1836, 4e. éd. t. ii. p. 14.

[†] Th. Schwann, *Arch. f. Anat. Phys. u. s. w.* 1844, p. 127.

[‡] I must refer to special physiological works for the method of setting up a biliary fistula in animals.

Westphalen's observations, already spoken of in the fourth chapter of this work, are those which have been made with the greatest care.[*] He collected the bile passed during every four hours of the day and night. The flow showed very little variation, saving that collected from 2 to 6 in the morning, which was always small. The other amounts, collected during the day, varied from 94·3 and 83·2 grm. in the four hours, while the bile collected in night and early morning was on an average only 61·8 grm. though it was the richest in solid constituents. Of these it held 2·499 *per cent.* while the bile secreted during the day was but a little over 2 *per cent.*

The highest quantity, secreted in four hours, seen by Westphalen was 125·2 grm.: the lowest 52·2 grm. The average about 83·9. Von Wittich in his case found the quantity secreted in four hours to be 88 C.C.[†] The results of the two observers thus nearly agree.

The quantity secreted every twenty-four hours in Westphalen's case was on an average of 10 days 498·85 grm. The highest quantity noted was 566·7 grm. The lowest 453·1 grm. Von Wittich estimates the amount in his case to be 532·8 C.C. Johannes Ranke gives 636 C.C. as the average of five observations in his case.[‡] These figures, however, are arrived at by allowing for the pulmonary mucus brought up with the bile. The sputa the day after the closing of the fistula amounted to 135 C.C. It is clear that Ranke's figures cannot claim strict accuracy, but only an approximation to truth. The highest number given by Ranke is 922 C.C. the lowest 405 C.C.

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[*] H. Westphalen, *Deutsches Arch. f. klin. Med.* 1873. Bd. xi. p. 588. See also above, p. 61.

[†] Von Wittich, *Arch. f. d. ges. Phys.* 1872, Bd. vi. p. 182.

[‡] Johannes Ranke, *Die Blutvertheilung*, Leipzig, 1871, p. 144.

There are some other cases also in which the amount of bile has been estimated, but perhaps not in so careful a manner, or with so much technical knowledge. In Dr. John Harley's case, a man of 29, the amount of bile lost from the fistula during a week was from 16 to 20 fluid ounces daily (440 to 560 C.C.) associated "with absence of bile from the alimentary canal"* which I suppose may mean that the fæces were free from colour. This amount of bile daily excreted would closely agree with that given by Westphalen, Johannes Ranke, and von Wittich.† Rouis, in a case of communication with the bronchi of an abscess in the liver, found that 900 grammes of a bilious fluid were brought up in 40 hours.‡ This statement, however, is but little worth; nothing definite is said of the state of the stools or of the amount of pus or mucus present.

In the two following cases, the amount of bile daily secreted was about half of what has been given above. Dr. Robinson found, in a woman of 64, whose stools were "destitute of bile," that the amount daily discharged through the fistula was about 8 fluid ounces§ (about 230 C.C.) And in Krumptmann's case, the fæces were grey white, yet the daily loss of bile is said to have been only between 7 or 8 ounces.*

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* John Harley, *Med. Chir. Trans.* 1866, vol. xlix. p. 89.

† Von Wittich, *Arch. f. d. ges. Phys.* 1872, Bd. vi. p. 181.

‡ Rouis, *Recherches sur les suppurations endémiques du foie*, Paris, 1860, pp. 139 and 424. Frerichs, with his habitual inaccuracy of quotation, says that the 900 grammes were collected within 24 hours. (*Klinik d. Leberkrankheiten*, Braunschweig, 1861, Bd. ii. p. 130.)

§ Robinson, *Med. Chir. Trans.* 1852, vol. xxxv. p. 472. The fluid was pronounced to be bile by Dr. Bence Jones.

In Westphalen's case, the amount of solids was on an average 2·25 *per cent.* varying from 3·856 to 1·844.

The patient weighed 68 kilogrammes; so that one kilogramme secreted in 24 hours 7·34 grm. of bile with ·166 solid matter.

In Johannes Ranke's case the amount of dry bile was found to vary from 2·69 *per cent.* to 4·01 *per cent.* figures much higher than Westphalen's, whose mean is 2·25 *per cent.*

The patient weighed 94lb. or 47 kilogrammes; so that one kilogramme secreted in 24 hours as *minimum* 8·61 C.C. of bile, containing ·25 grm. of solid matter; as *maximum* 19·62 C.C. of bile with ·8 grm. of solids.

The mean would be that one kilogramme secreted 14 grammes of fluid bile containing 0·44 gramme of solids in the twenty-four hours.

In Dr. Robinson's case the bile was noted to flow more copiously in the erect posture; probably this was due not to increased secretion but to a more rapid ejection. Dr. Robinson also says that the flow was more rapid after meals. In Westphalen's case, the chief meal was given in the middle of the day. On certain days the meal was put off for several hours, but no change in the amount or concentration of the bile was noted. On two days abundance of drink was given by the mouth; but no increased flow or marked dilution of the bile followed, while the urine was doubled in amount. A dose of calomel also was followed by no increase in the amount of bile. Quinine, given in doses of two grammes, (30 grains) could not be found in the bile.

This is all that I have been able to gather from direct observations on man. Observations upon animals, many of which have been made with very great care and accuracy, promise to give far wider information. It must first be said that Bouisson arrived, by methods which must be thought quite inadequate to this purpose, at the conclusion that the quantity of bile daily secreted was about 6 ounces or 192 grammes. He injected water from the liver into the intestine by the hepatic duct and found that the fluid divided itself into two equal parts; one passed into the intestine; the other into the gall bladder; the amount in the gall bladder was an ounce and a half or 48 grammes. The gall bladder empties itself, he says, twice a day; and thus the amount of bile daily secreted would be 6 ounces or 192 grammes, as stated above.*

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* Krumptmann, *Lond. Med. Record,* 1873, p. 264, quoted from *Wiener Centralblatt* for March, 1873.

Blondlot found that the dog on whom he had established a biliary fistula secreted daily about 40 to 50 grammes. He calculates from this that man would secrete from 200 to 250 grammes of bile daily.†

Hermann Nasse, the Professor of Physiology in the University of Marburg, made in 1847 with the assistance of Platner, the first attempt at any accurate estimation of the amount of bile daily secreted by the dog.‡ He found large fluctuations in the same dog on the same diet, observations which have been repeated by the latest authorities on the same matter, the Edinburgh Committee. Nasse's work is but little known in England, probably because it was published under the form of an academical dissertation, *ad novi Prorectoris inaugurationem*.

Bidder and Schmidt made an immense number of experiments both on beasts and birds. Beginning with cats, they passed on to dogs, comparing their observations on these carnivorous animals with experiments on sheep and rabbits, supplemented by some on the herbivorous goose and the carnivorous crow. They give the following table as the mean of their observations.*

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* Bouisson, *de la bile*, Montpellier, 1843, p. 54.

† Blondlot, *Essai sur les fonctions du foie*, Paris and Nancy, 1846, pp. 59 and 61.

‡ Herm. Nasse, *Commentatio de bilis quotidie a cane secreta copia et indole*, Marburg, 1851.

1 KILOGRAMME OF	CAT.	DOG.	SHEEP.	RABBIT.	GOOSE.	CROW.	
In one hour secretes in grammes	0·608	0·824	1·059	5·702	·491	3·004	Liquid bile.
	0·034	0·042	0·056	0·103	0·034	0·219	Dry bile.
In twenty-four hours secretes in grammes	14·5	19·990	25·416	136·84	11·784	72·096	Liquid bile.
	0·816	0·988	1·344	2·47	0·816	5·256	Dry bile.

This table represents the mean of observations made on the following plan: a biliary fistula was established, and as soon as the gall-bladder was emptied of all its bile, and the fresh secretion of the liver began to run, the whole of the bile passed during every quarter of an hour was received in weighed glass bulbs. At the end of three hours the animal was killed; the weights of the body, liver, fluid bile, and dry bile, were then compared. The biliary fistula was made an infinite variety of times; so long after a meal, or after so much food had been given, and an average struck of all these observations for the 24 hours, for each kilogramme of weight. An estimation made on such a method hardly recommends itself. As Claude Bernard has pointed out, the stature and size of the animal are left out of consideration.† And the weight of the entire body is not at all unimportant, for Heidenhain, by comparing Bidder and Schmidt's figures for sheep and rabbits, shows that as the weight of the whole body increases so the amount of bile for every kilogramme of body-weight decreases.

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* Bidder and Schmidt, *Die Verdauungssaefte*, Mitau and Leipzig, 1852, p. 209.

† Claude Bernard, *Leçons sur les propriétés &c. des liquides de l'organisme*, Paris, 1859, t. ii. p. 205.

	GUINEA PIG.	RABBIT.	SHEEP.
Mean weight.	518·400	1525·800	23377·000
Mean amount of bile for every kilogramme in one hour.	7·326	5·070	1·109

Now the smaller the animal the larger the liver, and *vice versa.* In guinea pigs, the ratio of weight of liver to whole body is 1: 27·3; in rabbits, 1: 33·5; in sheep, 1: 53·57. But this is not the sole cause; for 1 kilogramme of sheep's liver secretes 62·83 grm. in the hour; of rabbit's liver, 169·37 grm.; of guinea pigs, 185·54 grm: that is, the liver of guinea pigs secretes more, weight for weight, than those of either rabbits or sheep. And this is more striking if the following figures be compared: there is secreted every 24 hours by

	GUINEA PIG.	RABBIT.	SHEEP.	
Body . . .	$\frac{1}{5·6}$	$\frac{1}{8·2}$	$\frac{1}{37·5}$	times of own weight of fresh bile.
Liver . . .	4·467	4·064	1·507	

If, however, the amount of solids in the bile of the three animals be compared, altogether a different proportion is given. Of solid bile, each kilogramme of guinea pig secretes in the hour ·098 grm. each kilogramme of liver 2·67 grm. Of rabbits, ·103 grm.; liver, 3·74 grm. Of sheep, ·0672 grm; liver, 3·55 grm. So it is clear that the great amount of bile secreted by the guinea pig is due solely to a large amount of water. If the amount of fluid bile for each kilogramme of guinea pig and rabbit be compared, it is 7·326: 5·070; while the proportion of solid bile is 0·002: 0·103. A more than complete reversal of the proportion.

If, too, instead of a kilogramme of body-weight, the kilogramme of liver-weight be taken, the same is observed. One kilogramme of rabbit liver will secrete of fluid bile 169·37 in an hour, against 185·54 by guinea pig liver. Of solids, the rabbit liver secretes 3·74, against 2·67 by the guinea pig liver. Heidenhain thinks himself entitled to express the opinion, but not as a distinct doctrine, that when the amount of water passing from the liver is increased, the solids in the bile are decreased.[*]

A. Wolf agrees with Heidenhain as to the relation between the size of the liver and the amount of bile. He thinks that animals which are small and young, that is, whose liver is large, secrete more bile; and that the amount of the secretion is in direct ratio to the size of the liver. He has only, however, experimented on two young dogs.[†]

The views of the Edinburgh Committee are opposed to those of Heidenhain and Wolf. They found large variations in dogs which they could not explain either from the food or weight. They did not, however, make observations on the size of the liver, but they remark that it is improbable that this circumstance determines the amount of the biliary secretion, the great variation in the same animal from day to day being opposed to this.[‡] They give a table of the average amount of bile secreted by each kilogramme of dog. (see p. 104.)

Westphalen, from his direct experiment on man, found that one kilogramme produced 7·34 grammes of fluid bile, and 0·166 gramme of dry bile in the 24 hours.[§] Johannes Ranke found the mean much higher: one kilogramme produced 14 grammes of fluid bile, and 0·44 grammes of dry bile in the twenty-four hours.* This observer tries to bring this statement into agreement with the calculations which have been made from animals. Bidder and Schmidt found that one kilogramme in a cat secreted 14·5 grammes of fluid bile in the 24 hours, and one kilogramme in a dog 20—28 grammes. For the same animal Nasse found 12·2—28·4 grammes, figures which closely correspond with those of Bidder and Schmidt. Arnold's figures are smaller: 8·1 to 11·6 grammes;† while Kölliker and Müller's are larger: their *minimum* is 21·5 grammes of fluid bile, with 0·75 gramme of dry bile; their *maximum* 36·16, with 1·162 gramme of dry bile. All these are from observations on dogs. Johannes Ranke further observes that Bischoff and Voit in their observations on the same animal came to very nearly the same figure as Ranke did with man: one kilogramme of a dog excretes 0·43 gramme of dry bile, while one kilogramme of man excretes 0·44 grm of dry bile in the 24 hours, so that Ranke concludes that man excretes as a mean about 840 grammes of bile daily, with 20 grammes of solids. I must own that I do not feel any great confidence in Ranke's figures, as he shows a disposition to use the figures of observers when they corroborate his own; but to neglect them when they are against him. This is specially to be noted in his dealings with the amount of fluid and solid bile, when he passes from one to the other according as the figures fall into agreement with his own or not.

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[*] Friedländer and Barisch, *Arch. f. Anat. Phys.* 1860, p. 655.

[†] Wolf, *Uwagi nad fizyologia zôlci*, Warschaw, 1868. Abstract in *Centralblatt f. d. med. Wiss.* 1869, p. 86.

[‡] Bennett, Rutherford, and Gamgee, *Report of the Twenty-eighth Meeting of the British Association for the Advancement of Science*, London, 1869, p. 230.

[§] Westphalen, *Deutsches Arch. f. klin. Med.* 1873, Bd. xi. p. 600.

Dr. George Scott found, as an average of three days' observations on one dog, that each kilogramme of weight secreted 23·1 grm. of fluid bile, and 1·13 grm. of solid bile, in the twenty-four hours.‡ Ritter gives, as a mean of a week's observation on one dog, 17·5 and 18·75 grammes of bile to each kilogramme of weight in the twenty-four hours.* The Edinburgh Committee gives the following table of the mean amount of bile secreted by each kilogramme of the dogs which they observed :†

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* Johannes Ranke, *Die Blutvertheilung*, Leipzig, 1871, p. 151.

† All these figures are very conveniently given in a table put together by Kölliker and Müller (*Verhandlungen der phys. med. Gesellschaft in Würzburg*, 1856. Bd. vi. p. 461.) This table is given at p. 111, with some observations which have been published since 1856.

‡ George Scott, Beale's *Archives of Medicine*, 1857, vol. i. p. 218.

Number of Dog.	Fluid Bile. grammes	Solid Bile. grammes
1	6·47.	·412.
1	7·82.	·28.
2	5·27.	·34.
3	5·76.	·293.
4	3·53.	·146.
5	21·8.	·801.
6	20·66.	·818.
7	4·64.	·23.
8	9·24.	·305.
9	10·2.	·58.

The variations, even in observations made by the same observers, are here very great; and show how unsafe a course it is to draw conclusions from a small number of experiments.

The data for forming an opinion on the amount of bile secreted either in man or the beasts must be owned to be insufficient. The belief now prevalent among physiologists that the greater part of the bile is absorbed again by the intestines, and excreted again by the liver, must be taken into account. If this view be correct, it must be hard to arrive at any idea of the amount of bile in health by studying the amount passed out from a biliary fistula. The bile in this case is conveyed away out of the body, does not enter the intestine, and so cannot be absorbed, and again be excreted by the liver. To judge aright of the amount of bile, the quantity should be measured as it is secreted by the liver, and then passed again to the duodenum.

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* Ritter, *Einige Versuche ueber die Abhängigkeit der Absonderungs-Grösse der Galle von der Nahrung*, Diss. Inaug. Marburg, 1862, p. 11.

† Edinburgh Committee, *loc. cit.*

If we take Westphalen's mean, 500 C.C. as the normal flow from a biliary fistula, and the solids as a little over 2 *per cent.* the daily amount of solid bile will be about 10 grammes, or somewhat more.* Of these solid matters, the bile acids will form about one half; cholestearin and fats about one gramme; another gramme of pigments and mucus; while the remainder will be made up of inorganic salts; of which chloride of sodium is the greatly preponderating body, about 2·4 grammes being passed in the 24 hours. Johannes Ranke found the amount of solid bile in his patient nearly double these figures:† that is to say, of solid bile 20·6 grm. a day, of which the bile acids formed 11 grammes, the fat and cholestearin, the mucus and pigment, and inorganic ashes, all three, 3·2 grm. each. The sources of error which may have crept into Johannes Ranke's estimations, and which may have made it too high, have already been pointed out; but it is worthy of note that the figures correspond very nearly to the amount at which Ernst Bischoff calculated it in man from observations on animals.‡

Influence of food on the bile. It is commonly said, from experiments on animals, that the taking of food into the stomach is followed by an increase in the amount of bile. In Westphalen's patient, however, the chief meal was changed several hours, yet no apparent alteration in the amount or concentration of the bile followed.§ It is true that it was undesirable to allow this patient to fast, so that the immediate effect of food after a long abstinence could not be ascertained. In Dr.

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* Westphalen, *Deutsches Arch. f. klin. Med.* 1873. Bd. xi. p. 600.

† Johannes Ranke, *Die Blutvertheilung*, Leipzig, 1871, p. 150.

‡ Ernst Bischoff, *Zeitschrift f. rat. Med.* 1864, Bd. xxi. p. 141.

§ Westphalen, *Deutsches Archiv f. klin Med.* 1873, Bd. xi. p. 601.

Robinson's case it is distinctly stated that the flow was more rapid soon after meals.[*]

Blondlot, noted that the flow of bile in his dog, was much more abundant after food. When the animal was fasting, it sometimes, but not always, happened that several hours would go by without a drop of bile being passed; but if food were given, the bile would flow out in abundance at the end of 10 minutes or a quarter of an hour, and continue to flow throughout the time that digestion was going on.[†]

Claude Bernard taught that the secretion of bile took place after digestion was over. If you examine an animal with a biliary fistula, says he, you see that while the animal is fasting, nothing flows. If you give the creature food, the flow of bile does not begin at once, but at the end of a certain time, and it persists after digestion is finished. In fact, the bile of one digestion is only used in the next. The bile is collected in the bladder, which is emptied during digestion, but is filled before.[‡]

Bidder and Schmidt give the following as the result of their experiments on cats: the amount of bile is increased in the first hour after a meal, and before the food can have been absorbed into the blood. This is apparently simply a consequence of the increased flow of blood to the digestive organs. The increase of secretion reaches its highest point 12 to 15 hours after the meal have been taken, when it is probable that all the food has been completely digested and absorbed into the blood mass.[§] From this, the amount of secretion sinks; and in 24 hours after the meal, it has fallen below the amount which it showed immediately after the taking of food.*

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[*] Robinson, *Med. Chir. Trans.* 1852, Vol. xxxv. p. 473.

[†] Blondlot, *Essai sur les fonctions du foie*, Paris and Nancy, 1846, p. 62.

[‡] Claude Bernard, *Leçons &c. liquides de l'organisme*, Paris. 1859, t. ii. p. 202.

[§] The same year that Bidder and Schmidt's book was published, C. G. Lehmann expressed the opinion that more bile ought to be secreted 10 hours after food than 5 hours after; because there is more change in the blood later than earlier. (*Journal de Pharm. et de Chimie*, 1852, t. xxi. p. 399.)

Arnold states that he found the greatest amount of bile always to make its appearance in the first hours after the meal had been taken. The figures which he gives are as follows:†

1 hour	5·257 grammes.
2 hours	5·346 ,,
3 ,,	5·121 ,,
4 ,,	4·612 ,,
5 ,,	4·146 ,,
6 ,,	3·504 ,,
7 ,,	3·583 ,,
8 ,,	3·817 ,,
9 ,,	4·344 ,,
10 ,,	4·012 ,,
11 ,,	3·612 ,,

Arnold's experiments were made on one dog, and there appear to have been only two sets of observations on this point.

Kölliker and Müller find that a very small amount of bile is secreted in the first and second hour after food. Sometimes the amount is even less than in the 19th to 25th hour. In the 3rd to 5th hour, they found almost without exception an increase of the secretion. Indeed in two cases the fifth hour showed the highest amount, while in the others the *maximum* was seen from the 6th to 8th hour. After this, the amount again fell until the *minimum* was reached in the 19th to 25th hour.‡

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* Bidder and Schmidt, *Die Verdauungssaefte*, Mitau and Leipzig, 1852, p. 144.

† Friedrich Arnold, *Zur Physiologie der Galle*, Mannheim, 1854, p. 16.

‡ Kölliker and Müller, *Verhandlungen der phys.-med. Gesellschaft in Würzburg*, 1856, Bd. vi. p. 454.

Hour after food.	1st DOG.		2nd DOG		3rd DOG				5th DOG.	
					1st Series.		2nd Series.			
	Bile.		Bile.		Bile.		Bile.		Bile.	
	Liquid	Solid	Liquid	Solid	Liquid	Solid	Liquid	Solid	Liquid	Solid
1— 2	1·450	0.051	1·221	0·040	0·823	0·035	0·675	0.026	1·538	0·053
3— 5	1·407	0·047	1·462	0·042	1·198	0·044	0·986	0·034	2·222	0·060
6— 8	1·514	0·048	1·705	0·046	1·242	0·047	1·093	0·035	1.889	0·054
9—14									1·368	0·041
15—18									1·435	0·043
15—20					1·085	·040				
16—22	1·320	0·051								
19—21			1·119	0·036						
20—24									1·203	0.047
21—25							0·750	0·030		

The figures are grammes.

These observations of Kölliker and Müller seem to be certainly more worthy of confidence than those which went before them. They were made on the same animals, not as in Bidder and Schmidt's cases, on different animals at different times of digestion.

Voit, without giving further details, says that the observations, which he had made upon Bischoff's dog with a biliary fistula, showed that the secretion of bile rose immediately after taking nourishment. The *maximum* arrived in 2 to 4 hours. The solids of the bile were increased as well as the fluid part.*

In guinea pigs, it was noted by Heidenhain that no such great increase of the flow of bile took place after food. Nor did the flow seem much decreased by fasting. It was only when the guinea pig had fasted for 66 hours that any decrease was noted. The guinea pig is a vegetable eater, and his stomach remains full of food long after the last meal: so the process of digestion is always going on, and in this way Heidenhain explains the difference between flesh eaters and vegetable eaters.*

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* Karl Voit, *Phys.- chem. Untersuchungen*, Augsburg, 1857, p. 41.

Some experiments of Ritter's are an attempt to reconcile the varying statements of other observers. He made six observations on his dog and gives the following as the result of his labours on this point: that after food there are two *maxima* of secretion of bile; the former of these falls in the first or second hour after the meal; the latter has no such precise time of appearance; the less the amount of nourishment, the earlier its appearance; the greater, the later.†

Influence of the amount of food on the bile.—It has been seen that Kölliker and Müller found the amount of bile to fall to its lowest point, 19 to 25 hours after a meal; Bidder and Schmidt saw that by withholding nourishment from cats the amount of bile sank to a *minimum;*‡ 240 hours after the last meal, the amount of fluid bile was only 94 milligrammes in an hour, and of solid bile but seven milligrammes.

The Edinburgh Committee saw a marked effect follow the withholding of food from a dog. Only liver was given as food, and no water; the amount of bile fell to 104·8 grammes in the 24 hours against 140 grammes for the two foregoing days. The bile solids, however, rose to 7·73 grammes, about one half more than they had been; and this was due to a great rise in the organic constituents of the bile as the inorganic salts remained the same in amount. The next day, only water was allowed, and the amount of fluid bile fell to 41·6 grammes, and the solids to 2·77 grammes.§

From these observations it may be looked upon as a probable opinion that the withholding of food decreases the amount of fluid bile secreted, and possibly also of the solid bile.

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* Friedländer and Barisch, *Arch. f. Anat. Phys.* 1860, p. 654.

† Joseph Franz Ritter, *Einige Versuche über die Abhängigkeit d. Absonderungs-Grosse der Galle von der Nahrung*, Diss. Inaug. Marburg, 1862, p. 27.

‡ Bidder and Schmidt, *op. cit.* p. 144.

§ Edinburgh Committee, *op. cit.* p. 222.

Bidder and Schmidt also fed two cats abundantly with meat; one took in four days no less than a half of its own weight; the other took one-third of its own weight in two days. The amount of bile secreted by each animal was almost the same. For every kilogramme of cat, there was secreted in one hour, in the first cat, 2·055 grm. of fluid bile with ·172 grm. of solids, and in the second cat 1·965 of fluid bile with ·178 grm. of solids. The average which they give for cats is that one kilogramme secretes in every hour ·608 grm. of fluid bile with 34 milligrammes of solids. So that if these two experiments on cats represent a general rule, a great increase in the secretion of bile takes place on an abundant diet.

In Arnold's experiments, the dog, weighing 7·75 kilogrammes, was fed daily with 750 grm. of meat. The amount of bile daily secreted was on an average 90·295 grm. One kilogramme of the dog, therefore, on this diet of meat secreted 11·65 grm. of bile in the 24 hours. One gramme of bile was secreted in twenty-four hours for every 8·306 gramme of meat given. When the same dog was daily fed on 470 grm. of rye bread, the weight of the dog being 7·812 kilogramme, there was secreted of bile on an average 63·024 grm. Therefore on this amount of rye bread one kilogramme of the dog secreted 8·067 grm. in the 24 hours. One gramme of bile was secreted in the twenty-four hours for every 7·459 gramme of bread given.*

The following table has been drawn up by Kölliker and Müller and is a convenient summary of what was done by these observers and those who had gone before them, of the amount of bile secreted under differing

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* Friedrich Arnold, *Zur Physiologie der Galle*, Mannheim, 1854, p. 16.

Name of Observer.	For every kilogramme of dog there was secreted in 24 hours:		Food for every kilogramme of weight.	For every 100 grammes of food in the 24 hours there was secreted of	
	Fluid Bile	Solid Bile		Fluid Bile	Solid Bile
	Grammes.		Grammes.	Grammes.	
1. Nasse.	19·2	0·685	155 flesh meat	12·3	0·440
2. „	22·8	0·700	208 „ „	11·01	0·337
3. „	23·1	0·784	260 „ „	8·9	0·300
4. „	24·0	0·765	meat *ad lib.*	——	——
5. „	28·4	0·760	„ „ „	——	——
6. Arnold.	11·6	0·373	75 flesh meat	12·0	0·385
7. Kölliker & Müller.	32·7	1·034	——	——	——
8. „ „	32·6	1·290	98 flesh meat	——	——
9. „ „	26·1	1·013	92 „ „	28·56	1·094
10. „ „	21·5	0·748	94 „ „	22·85	0·792
11. „ „	36·1	1·162	64 „ „	56·50	1·816
12. „ „	53·6	1·683	94 „ „	56·7	1·79
13. Bidder & Schmidt.	15·9	0·840	32 „ „ 1·7 fat	49·3	2·608
14. „ „	16·7	0·696	17 flesh 7·8 milk	83·5	3·48
15. „ „	24·5	1·176	79 flesh 8 bread	25·7	1·23
16. „ „	28·7	1·268	66 flesh 8 bread	35·1	1·54
17. Nasse.	17·7	0·446	100 flesh 100 bread	——	——
18. „	17·9	0·400	130 flesh 100 bread	——	——
19. „	12·2	0·505	87 „	13·9	0·575
20. Arnold.	8·1	0·215	60 „	13·4	0·353
21. Kölliker & Müller.	32·1	——	37·9 bread 94 c.c. milk	——	——
22. Carl Voit. . . .	11·8	0·503	48·2 flesh	24·5	1·115
23. „ „ . . .	10·8	0·5	54 „	20·0	0·914
24. Dr. George Scott.	23·1	1·13	62·7 flesh 70 milk		
25. Ritter.	18·75		183·4 flesh	10·22	
26. „	17·5		170·6 „	10·29	
27. „	15·2		138·8 „	11·007	
28. „	13·4		103·5 „	13·10	
29. „	10·5		70·5 „	14·81	
30. Edinburgh Committee. . . .	6·47	0·412	12·3 dry food	52·18	3·32
31. „ „	7·82	0·28	13·6 „ „	57·21	2·05
32. „ „	5·27	0·34	6·7 „ „		
33. „ „	5·47	0·293	10·9 „ „	58·9	3·165
34. „ „	3·53	0·146	8·8 „ „	40·13	2·148
35. „ „	21·8	0·801	23·4 „ „	92·9	3·49
36. „ „	4·64	0·23	19·34 „ „	23·99	1·21
37. „ „	9·24	0·305	9·3 „ „	51.84	1·714

amounts of food.* The figures of the authors since 1856 have been put together for this work.

Kölliker and Müller say very truly that on first looking through this table it does not seem possible to draw any general conclusions from it. They think that there is a certain correspondence, however, between the conclusions of Nasse and Arnold on the one side; and Bidder and Schmidt with Kölliker and Müller on the other. The two first authors find the amount of solid bile secreted by one kilogramme of dog in 24 hours, on different kinds of food, to vary between 0·215 and 0·785 grm.; the latter observers find it between 0·696 and 1·290 grm. If, however, the amount of fluid bile secreted in the 24 hours for every kilogramme of dog be compared, a different aspect is given to matters; Nasse gives it as from 12·2 to 28·4 grm.; and Bidder and Schmidt between 15·9 and 28·7: a close correspondence. But the solid bile is that which is of most importance; and the higher figures of Nasse correspond to a higher amount of food, while the dogs of Bidder and Schmidt were fed rather low. The dogs of Kölliker and Müller were, however, better fed than those of Bidder and Schmidt, yet the amount of dry bile in Bidder and Schmidt's dogs was nearly on a level with Kölliker and Müller's. It would follow that the observations of these four writers have a real correspondence with each other. This is still more marked, as is also the agreement between Arnold and Nasse, when the amount of bile secreted for each 100 grm. of food is considered. Nasse and Arnold give between 8·9 and 13·9 grm. of fluid bile with 0·300 to 0·575 dry bile for every 100 grm. of food. Bidder and Schmidt with Kölliker and Müller on the other hand give much higher figures: 22·85 to 83·5 grm. of fluid bile with 0·792 to 3·48 of dry bile to every 100 grm. of food.

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* Kölliker and Müller, *Verhandlungen d. phys. med. Gesellschaft in Würzburg*, 1856, Bd. vj. p. 461.

I am more inclined myself to agree with the first paragraph of Kölliker and Müller's argument, and to think that but few general conclusions can be drawn from this table, even if the more recent observations be taken into the service. The variations in the figures of the Edinburgh Committee are very considerable; a large amount of bile was secreted when either little or much food was given.

Ritter, a pupil of Nasse, made under his guidance many careful and interesting observations on a dog, in whom he had established a biliary fistula. He found that by decreasing the daily amount of food, the amount of bile also decreased.* For example: the dog, fed on 2500 grm. of meat daily, produced on an average 255·5 grm. of bile in the 24 hours. Fed only on 1000 grm. of meat daily, he produced 147·1 grm. of bile in the 24 hours. The following table shows the exact figures:

WEIGHT OF DOG BEFORE THE BILIARY FISTULA WAS ESTABLISHED = 13·5 KILOGRAMMES.

Series of experiments.	Food in fresh meat.	Average weight of animal.	Average amount of bile in 24 hours.	Average secretion of 1 kilogramme in 24 hours.	Amount of food in meat for every kilogramme of the dog in 24 hours.	For every kilogramme of meat there were secreted in 24 hours, of bile.
1.	2500	13·629	255.5	18·75	183·4	102·2
2.	2500	14·656	257·3	17·5	170·6	102·9
3.	2000	14·52	220·15	15·2	138·8	110·07
4.	1500	14·544	196·5	13·4	103·5	131·0
5.	1000	14·175	148·1	10·5	70·5	148·1

The weights in this table are in grammes.

The first series of experiments lasted uninterruptedly for 7 days: the second for 8 days: the third for 5 days: the fourth also for 5 days, but with an interlude of 3 days between the 2nd and 3rd day of observation; the fifth for 4 days without interruption.

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* Joseph Franz Ritter, *Einige Versuche über die Abhängigkeit der Absonderung Grösse der Galle von der Nahrung*, Diss. Inaug. Marburg, 1862, pp. 10, *et seqq.*

Influence of the kind of food upon the secretion of the bile.—Bidder and Schmidt fed two cats only on fat or oil for five or three days, and a third was fed abundantly for several days on very fat meat. The first cat yielded by kilogramme in an hour 0·688 to 0·128 grm. of liquid bile, and 62 to 16 milligrammes of solid bile; the second, 0·347 to 0·211 grm. of fluid and 39 to 15 milligrammes of solid bile. The third cat, fed on very fat meat, yielded 0·327 to 0·181 grm. of fluid bile and 28 to 16 milligrammes of solid bile.* These figures are very little above, if not equal to, those given by cats who had fasted for days. It follows that, in animals fed solely on fat, the secretion of bile falls to a *minimum*. These observers also noted that those animals, with little fat under their skin, often gave a more abundant secretion of bile than fat ones.†

Yet, according to some experiments of Nasse, it would seem that if fat be added to the ordinary food, the amount of bile secreted is raised. For five days he fed a dog with meat and fat, and the secretion attained the amount of 219·8 grm. in 24 hours. The same amount of meat, but without the fat, was given for the five following days, and the secretion fell to 59·26 in the 24 hours. Then he gave fat, as much as the animal would take with the other food, for four days; and the amount of bile rose again to 206·13 in the 24 hours. The bile soon after fell again in amount, as the creature lost its appetite and refused its food.‡ The dog was therefore probably out of health during the observations.

Ritter has continued some observations in the same direction, but without the striking results obtained by Nasse. He did not, however, feed his animal for several days without or with fat: but gave fat about every alternate day. There is but little variation in the amount.*

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* Bidder and Schmidt, *op. cit.* p. 148.

† p. 236.

‡ Hermann Nasse, *Commentatio de bilis quotidie a cane secreta copia et indole*, Marburg, 1851, p. 14.

DATE.		FOOD.	GRAMMES OF BILE IN 24 HOURS.
Dec.	26.	1000 grm. of meat without fat.	170·3
	27.	same with 125 grm. of hog's-fat.	213 grm.
	28.	same.	212·3
Jan.	11.	1500 grm. of meat without fat.	182·6
	12.	same.	207·2
	13.	same with 125 grm. of hog's-fat.	180
	14.	same.	202·8
	15.	same without fat.	216·8
	16.	750 grm. meat without fat.	171·0
	17.	same.	162·8
	18.	same.	124·1
	19.	same with 125 grm. of hog's-fat.	132·0
	20.	same.	138·6
	21.	same without fat.	130·6
	22.	same.	123·6

The belief that fat joined to other food causes an increase of bile is not supported by these figures.

The last experiments made by Ritter were the substitution of potatoes for flesh in the diet of his dog; the amount of bile at once sank and continued low, whether fat were or were not given with the potatoes. The amount of bile secreted in the twenty-four hours varied in four experiments from 46 to 66·1 grm.†

The observations of Arnold, who found a lower amount of bile secreted when the dog was fed on rye bread than when fed on meat, have already been quoted. The proportion for each kilogramme was 11·65 grm. of bile on flesh, to 8·667 on bread,‡ a considerable decrease.

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* Ritter, *Einige Versuche über die Absonderungs-Grösse der Galle von der Nahrung*, Diss. Inaug. Marburg, 1862, p. 28.

† Ritter, *op. cit.* p. 32.

‡ Arnold, *Zur Physiologie der Galle*, Mannheim, 1854, p. 16.

And Karl Voit found about the same amount as Arnold when his two dogs were fed only on meat; 11·77 and 10·77 grm. of bile secreted by the kilogramme in the 24 hours.*

If the figures of Ritter be looked through, it is evident that most bile was secreted when the animal was most abundantly supplied with flesh. He does not seem to have tried feeding the animal with an equal weight of bread. When fed with potatoes in weight equal to that of meat, the secretion certainly fell very much lower (4: 1).

In looking at the table from Kölliker and Müller, it is hardly possible to draw any conclusion; if anything, the figures would seem to show that as much solid bile is secreted on a low diet as on a full one. The highest amount of solid bile secreted was when the dog was fed on but 17 grm. of meat, and 7·8 of milk for every kilogramme.

It would seem *à priori* probable that more bile should be secreted on a high than a low diet, and also that a nitrogenous diet should favour the secretion, as the bile acids contain so much nitrogen. The whole of Ritter's experiments are rendered much less valuable by his neglect of the solid constituents of the bile; a troublesome estimation, it will be owned, but one which cannot be avoided in investigations of this sort.

Difference between night and day.—Westphalen noted in his patient that the lowest amount of fluid bile in the twenty hours was always secreted in the night, between 2 and 6 a.m. It contained, however, a far larger percentage of solids.† Nasse had before remarked that in the dog the amount of bile was less at night than in the day, although if the dog were fed night and morning instead of at mid-day, or had taken a great quantity of food, this decrease was not noticed. During the night it appears that the percentage of solid matters was usually greater than during the day.[*] Ritter, Nasse's pupil, repeated this observation in 1862.[†]

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* Karl Voit, *Phys.-Chem. Untersuchungen*, Augsburg, 1857, pp. 38 and 40.

† Westphalen, *Deutsches Arch. f. klin. Med.* 1873, Bd. xi. p. 595.

Influence of drink on the secretion of the bile.—In Westphalen's patient no increase in the bile followed the drinking of a considerable quantity of water on two following days. There was no noteworthy dilution of the secretion, although the amount of urine was doubled, and its specific gravity sank from 1021 to 1011.[‡] On animals, however, quite the opposite has been seen. Bidder and Schmidt noted that in three dogs the amount of bile was doubled or trebled very shortly after drink was given; not merely the water but the solid contents of the bile were increased.[§] In one dog, however, this result did not always take place; for out of five experiments it was not seen in two and but slightly in one.[‖]

Nasse reports shortly that if the dog took a great quantity of water with the food, there was a larger secretion of bile.[¶] Arnold says the same thing.[**]

Röhrig also found, both in dogs and rabbits, that the injection of warm water into the small intestine had a marked effect on the amount of secretion. The effects of a second injection were more lasting than of the first.[††] Only the amount of bile was estimated in Röhrig's experiments, not the solid contents.

Mosler injected water into the veins, but no account is given of the amount of the secretion if increased or decreased.[‡‡]

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[*] Nasse, *Comment de bilis quotidie, etc.* Marburg, 1851, p. 19.

[†] Ritter, *Einige Versuche u. s. w.* Diss. Inaug. Marburg, 1862, p. 23.

[‡] Westphalen, *Deutsches Arch. f. klin. Med.* 1873, Bd. xi. p. 600.

[§] Bidder and Schmidt, *op. cit.* pp. 166 and 168.

[‖] p. 181.

[¶] H. Nasse, *Commentatio de bilis quotidie, etc.* p. 18.

[**] F. Arnold, *Zur Physiologie der Galle*, Mannheim, 1854, p. 17.

[††] Röhrig, Stricker's *Med. Jahrbb.* Wien, 1873. p. 246.

[‡‡] Mosler, *Arch. f. path. Anat.* 1858, Bd. xiii. p. 32.

Prince Tarchanoff injected 200 C.C. of distilled water into the jugular vein of a dog and found a great increase in the amount of fluid bile and of the pigment.[*]

Socoloff, in two experiments also made in Hoppe-Seyler's laboratory, came to results which agree with those of Westphalen rather than with those of Bidder and Schmidt and the other observers. He injected 50 C.C. of 1 *per cent.* solution of common salt into the stomach of a dog, and 100 C.C. of a like solution into the crural, later on. Rather a fall than an increase was noted, especially in the second case, both in the amount of fluid and solid bile.[†]

Heidenhain agrees with Bidder and Schmidt that an increase of bile takes place in most cases; but not in all. Out of ten there were two in which no increase of the flow took place.[‡]

Influence of an increase or decrease of the blood pressure in the liver on the secretion of bile.—Heidenhain, with the assistance of his two pupils, Körner and Strube, found that the sudden raising of the blood pressure by injecting $\frac{1}{20}$ or $\frac{1}{40}$ of their weight of water into the veins of guinea pigs, caused in the first hour a decrease in the amount of bile. The decrease was always present in the first hour, and in 4 of the 7 experiments lasted for some hours, while in three experiments it soon began to rise again. In these four experiments the fall was considerable; it was smaller in the last three.

On lowering the blood pressure by bleeding the guinea pig, or by tying one of the mesenteric veins or the splenic vein, there followed a like decrease in the amount of bile collected.[§]

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[*] Johannes, Fürst Tarchanoff, *Arch. f. d. ges. Phys.* 1874, Bd. ix. p. 330.

[†] Socoloff, *Arch. f. d. ges. Phys.* 1875. Bd. xi. p. 176.

[‡] Körner and Strube, *Studien d. phys. Inst. zu Breslau*, Leipzig, 1863, Heft ii. p. 94.

[§] Heidenhain, *Studien d. phys. Instit. zu Breslau*, Leipzig, 1863, Heft ii. p. 94. Cf. below (p. 122.) the important experiments on irritation of the spinal chord, and and consequent changes in the blood pressure in the liver.

Hermann Nasse says that no change in the secretion of the bile followed the loss of a "few ounces" of blood from the jugular vein.[*]

Johannes Ranke found that the secretion of bile in a guinea pig absolutely stopped when the creature had lost ⅓ of the weight of its blood.[†] He also says that the secretion begins again if fluids be injected into the veins after this loss of blood.[‡] Röhrig found the secretion of bile in two dogs to be brought to an end by a bleeding; the injection of water into a mesenteric vein again made the secretion to flow, but only for a very few seconds.[§]

Influence of the contractions of muscles on the secretion of bile.—The relation of bodily exercise, or of the contraction of muscles, to the metamorphoses of the tissues is one of the most interesting problems in physiology. Johannes Ranke has attempted to make out the influence of muscular contraction on the bile, and comes to the conclusion that the change in the distribution of blood to the muscles corresponds to a change in the functions of the liver; and that when the muscles from their contraction contain more blood, less blood flows to the liver, which therefore does less work; thus the muscular contraction has all the effect of bleeding.[‖] Johannes Ranke's experiments seem somewhat open to criticism. The intestines were considerably interfered with, and a disturbance in the circulation might thus be readily set up. And the application of the electricity seems to have followed at very short intervals, so that it would be hard to distinguish between the effects of the contraction and exhaustion of the muscles.

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[*] Hermann Nasse, *Commentatio de bilis quotidie a cane secreta copia et indole.* Marburgi, 1851, p. 12.

[†] Johannes Ranke, *Die Blutvertheilung*, Leipzig, 1871, p. 190.

[‡] p. 117.

[§] Röhrig, Stricker's *Med. Jahrbb.* Wien, 1873, p. 246.

[‖] Johannes Ranke, *op. cit.* p. 117.

Inspiratory movements and struggles are noted by many writers as causing an increased flow of bile from a biliary fistula: so vomiting. These phænomena are not due to an increased secretion, but, the pressure within the belly being raised, the bile already secreted and in the ducts is expelled. The Edinburgh Committee noted an increased flow of bile during the first half hour that the dogs were taken from their cages and let run about.[*]

Influence of the nerves on the secretion of bile.—Schiff divided in dogs and cats the nerves which accompany the hepatic artery, but found no change in the secretion of bile.[†] Röhrig found no change on division or irritation of the *vagus*.[‡]

Heidenhain's pupils, Goldschmidt, Hausmann and Lissa, found that in guinea pigs a considerable decrease in the secretion of bile followed the section of one or both *vagi*. But the disturbances which section of the *vagus* sets up are many. One of them is a very slow breathing; and it was found that when artificial respiration was used the amount of bile evacuated by the fistula at once rose, but not quite to the normal amount. If, however, only one *vagus* be divided, it is sometimes long before the slow breathing appears. In two cases this was noted; in one of these the amount of bile was unchanged; in the other it sank somewhat. But little can be inferred from these experiments; and it was next determined to divide the *vagi* below the diaphragm, after the branches to the lungs had been given off, and to irritate the nerves below the diaphragm. In making the biliary fistula a ligature was placed on the gullet below the diaphragm, so that the *vagi* could readily be compressed. The amount of bile fell, but not very markedly. Electrical irritation of the *vagi* was followed by no remarkable increase in the amount of the secretion of the bile. It may be concluded that the *vagi* have no immediate influence on the bile; but the changes which are seen are due to slow breathing, drawing of blood from the liver into the chest, decrease of movement in the portal system, or increase of the heart's action, all of which tend to beget a passive congestion of the liver.[*]

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[*] Edinburgh Committee, *Report of the Thirty-eighth Meeting of the British Association for the Advancement of Science; held at Norwich in Aug.* 1868. Lond. 1869, p. 231.

[†] Schiff, Canstatt's *Jahresbericht f.* 1862, Bd. i. p. 126, quoted from *Schweizersche Zeitschrift f. Heilkunde*, 1862, Bd. i. 1862, p. 1.

[‡] Röhrig, Stricker's *Med. Jahrbb*, 1873, p. 258.

Pflüger, without giving details, shortly reports that he has cut through the *vagi*, phrenics, splanchnics, and sympathetics, has destroyed the cœliac plexus, has crushed all the nerves entering the porta, and yet found the secretion of the bile to continue as before. From this he draws the inference that the liver possesses a nerve centre within itself. Irritation of the *vagi*, splanchnics, cœliac plexus, and the portal nerves, gave no result. If the liver itself be irritated with electricity for one or two minutes, the flow of bile becomes very slow, or even leaves off altogether, for as much as 10 to 20 minutes. Pflüger thinks that this appearance cannot be explained by supposing a contraction of the vessels or bile ducts.[†]

Some very interesting experiments were also made by Freundt and Graupe in Heidenhain's laboratory; they found no change in the amount of fluid bile or bile solids after the diabetic puncture had been made on 9 guinea pigs.[‡]

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[*] Heidenhain, *Studien d. phys. Instituts zu Breslau*, Leipzig, 1863, Heft. ii. p. 82.

[†] Pflüger, *Arch. f. d. ges. Phys.* 1869, Bd. ij. p. 191. Pflüger ends his paper with the words: "Bald Ausführlicheres," but I do not know of any paper published afterwards in which the details necessary for forming a judgment on the results are given.

[‡] Heidenhain, *op. cit.* p. 69.

Heidenhain and his pupils found that, on irritating the spinal chord at the level of the third or fourth cervical vertebræ, the amount of bile was decreased. In the one experiment given to us as a specimen, the bile was reduced almost one half. The spinal chord was irritated by needles inserted into the neck, along which electricity was sent by means of a magnet electromotor. The animal showed several contractions of the muscles during the time of irritation. But if these observations be looked at a little attentively, it is seen that there were two periods; one, at the very beginning of the irritation, in which the secretion seemed hastened; and a second, following the first, in which the secretion was decreased. Casting about for an explanation of these two appearances, it seemed to Heidenhain that the first might be explained by supposing an increased flow of bile, a mere driving out of material already formed; and the second, by supposing a narrowing of the intralobular ducts, which would thus cause a hindrance to the descent of bile formed. Or, as the branches of the mesenteric and hepatic arteries contract forcibly when the spinal chord is irritated, it might be that the blood pressure in the capillaries of the liver would sink, and thus a true decrease of the secretion of bile take place.

In deciding between these two hypotheses it must be considered that if there be a narrowing or contraction of the gall ducts, there would be no tendency of fluid to flow back into the liver, when a tube filled with fluid is connected with the common duct, and the tube placed horizontally, either on a level with the duct, or but slightly above it, so as to exert but small pressure. During the first period of irritation of the spinal chord, the fluid in the tube remained either stationary, or was pushed somewhat forward. During the second period, the fluid ran back into the liver: so that the hypothesis of a contraction of the ducts had to be given up. Now this flowing back of the bile into the liver might be due to three things: (i.) a decrease of secretion; (ii.) an increase of absorption; or (iii.) a combination of both these circumstances. The bile, however, runs back too rapidly for the appearance to be due solely to a decrease of the secretion only. It must therefore be an increase of absorption. To what is this increase of absorption due? Heidenhain answers: to a decrease of the blood pressure in the capillaries of the liver, and points out that Frerichs had already formulated such a theory of jaundice.* Heidenhain brings forward experiments made by his own pupils, Kube and Szostokowski, which show that, after a general bleeding, the bile is readily absorbed by the gall ducts. By again injecting blood into the veins, the absorption becomes less. Max Heidenhain and Lichtheim, also, lowered the blood pressure in the liver by compressing the aorta in rabbits after the arteries to the head had been given off, and found the same result. With compression, the bile was absorbed; during the intervals of compression, it flowed out of the ducts.† The likeness of the states caused by irritation of the spinal cord, and by mechanically inducing a lowering of the blood pressure in the liver is thus manifest. The contraction of the small arteries is a necessary part of both. Kube and Szostakowski have also made experiments in which they estimated the blood pressure in the carotid at the same time that they noted the changes in the flow of bile. They found the flow of bile to decrease only when a great increase of pressure was seen in the large arteries; that is, when the smaller arteries were contracted, and therefore, the pressure in the capillaries was small.

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* Frerichs, *Klinik d. Leberkrankheiten*, Braunschweig, 1858, Bd. i. p. 89-94.

† See Ranke's experiments above, p. 119.

The appearance of an increase in the flow of bile, during the first period of irritation of the spinal chord, Heidenhain finds it more difficult to explain. He falls back upon his old belief in a contractility of the gall ducts. He does not believe that there is any increase of secretion, but the appearances seen in his experiments rather suggest that the secretion already formed is shot out of the ducts during the first period. Then he gives histological reasons for thinking that the gall ducts contain contractile elements.* Another motive is the irregularity of the appearance of the secretion which may often be noted in animals left to themselves. Heidenhain ends his paper by the notes of another experiment on compression of the aorta and outflow of bile. The flow of bile was great during the time of compression. Heidenhain sets this down to the contractility of the gall ducts, because the muscular coat of the bowels and the uterus contract under like circumstances.†

Another explanation of this first period may be given. The blood vessels and gall ducts lie close together in the portal spaces in the liver. Any increase in the one must cause a decrease in the size of the other. If, before the contraction of the small arteries begin, there be a dilatation of them, as seems quite likely, there will be a pressure exerted upon the ducts corrresponding to the dilatation of the blood vessels. This would account at once for the apparent increase of the flow of bile, and for the appearance which Heidenhain has noted that it was, as it were, shot out of the ducts.

Röhrig in the course of his research, made an attempt to repeat Heidenhain's experiments on irritation of the spinal chord. He did not use the same method of irritation, and it is plain therefore, that his results may not be compared with those of Heidenhain. In a dog and two rabbits, he irritated with electricity the crural and sciatic nerves, but he altogether missed the first stage of increased flow, and saw only the second stage, that of decreased flow.[*]

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* For a discussion of this question and the neighbouring one of *icterus spasticus*, see the chapter in this work on *icterus simplex*.

† Heidenhain, *Studien des phys. Instituts zu Breslau*, Leipzig, 1868, Heft iv. pp. 226-246.

J. Munk has repeated these experiments, both in Heidenhain's way and in Röhrig's way, and comes to the conclusion that Heidenhain's observations are right, and that Röhrig is mistaken.[†]

Röhrig, being led to the assumption that hyperæmia of the bowels and liver corresponded to an increase in the activity of the liver, determined to watch the effect of cutting the splanchnic nerves. He only did this experiment twice; and this in two dogs already at the point of death from other experiments. The division of the nerves was followed by some increase in the amount of bile, but ceased in a few seconds with the life of the animal.[‡]

Munk repeated Röhrig's experiment of dividing the splanchnics in rabbits; and found that the flow of bile was first hastened, then made slower. Assuming that the splanchnics contain the greater part of the vaso-motor nerves of the liver, and also the nerves which, according to Heidenhain's belief, supply the muscular coat of the gall ducts, it would follow that after dividing the splanchnics, irritation of the spinal chord would not be followed by any change in the flow of bile. This assumption was verified by experiment. Reflex irritation of the spinal chord of a rabbit was set up by the irritation of the sciatic nerve; and as a consequence, first a quicker, and then a flow of bile slower than natural took place. The splanchnics were then divided, and the sciatic nerve again irritated, but no change in the flow of bile was noted.*

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[*] Röhrig, Stricker's *Med. Jahrbb.* Wien, 1873, p. 259.

[†] J. Munk, *Arch. f. d. ges. Phys.* 1874, Bd. viii. p. 151.

[‡] Röhrig, *op. cit.* pp. 257 and 258.

Röhrig found in two rabbits that division of the spinal chord high up in the neck was immediately followed by a great increase of the flow of bile, then a decrease, and the secretion finally ceased with the death of the animal. In a third rabbit, already used for other experiments of compression of the vessel, this method of death caused a slight increase in the flow.†

Influence of the ligature of certain vessels.—The effects of ligature of the portal vein or hepatic artery have already been discussed,‡ and Heidenhain's results after compressing or tying the aorta have been spoken of.§

Röhrig found that complete ligature of the aorta close to the diaphragm in a dog and a rabbit was followed at once by a decrease in the flow of bile. Digital compression did not give the same result. Ligature of the aorta, after the cœliac had been given off, caused at first a slight increase in the flow of bile which became weaker and weaker, as the place of ligature was moved farther down.

The same observer found that ligature, complete or incomplete, of the vena cava, at some point between the left auricle and the hepatic veins, caused a decrease if not a stoppage of the flow of bile.

Röhrig comes to the conclusion that the secretion of bile is not altogether dependent on the blood pressure in the liver. The blood pressure is increased when the aorta below the cœliac is tied, and yet there was a slight increase in the flow of bile; there was a complete stoppage of the flow when the blood pressure was raised by tying the inferior cava.[*] It seems to me that the two experiments ought not to be compared.

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* J. Munk, *Arch. f. d. ges. Phys.* 1874, Bd. viii. p. 160.

† Röhrig, *op. cit.* p. 258. The results of Röhrig's experiments are rendered much less valuable from a scientific point of view by his custom of using one animal for two experiments.

‡ See p. 87.

§ See p. 124.

Effects of irritation of the digestive canal.—Röhrig has irritated the mucous membrane of the mouth, tongue and stomach, of the duodenum and large and small intestines, the peritonæum, by means of ammonia and acetic acid, and weak or strong electrical currents, and yet seen no change in the flow of bile. In a few experiments he thought that dropping a little ammonia on the tongue, or pinching it with a forceps, called forth a momentary increase. He has never, however, seen the least change, with any agent, follow irritation of the duodenum: acetic acid, dilute hydrochloric or sulphuric acid.[†] It should be remembered that Claude Bernard noted that if the orifice of the bile duct into the duodenum were touched with weak acetic acid, immediately a rush of bile poured into the intestine. Nothing of the sort, however, happened if instead of acetic acid, a slightly alkaline fluid were used, as for example, carbonate of soda.[‡] Now Tiedemann and Gmelin always found the gall bladder empty in animals during digestion, and they explain this on the theory of an irritation of the duodenum by the chyme. No doubt they are right in this view. The acid chyme, passing over the papilla, causes a flow of bile as in Bernard's experiment.

Röhrig injected the contents of the stomach and small intestine of a dog, who had been well fed, into the stomach of another dog. There was a much greater increase in the amount of bile than when mere water was injected. A result that might be expected.

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[*] Röhrig, Stricker's *Med. Jahrbb.* Wien, 1873, p. 243.

[†] Röhrig, *ibid.* p. 248.

[‡] Claude Bernard, *Leçons de physiologie expérimentale*, Paris, 1856, t. ij. p. 429. This experiment has been repeated and confirmed by Küthe (*Zur Function der Leber*, in Heynsius' *Studien des. phys. Inst. zu Amsterdam*, Leipzig and Heidelberg, 1861, p. 38.) Cf. Tiedemannn and Gmelin, *Recherches*, etc. Paris, 1827, partie i. p. 375.

He found that during diarrhœa the flow of bile was very abundant.[*] The exposure of the intestines to the air was also followed by some increase of the secretion.

H. Nasse, however, had noted in 1847 that in diarrhœa the amount of bile was decreased,[†] and the Edinburgh Committee,[‡] in 1868, and Dr. Rutherford later on, after Röhrig's experiments, did not find that active purging increased the secretion of bile. "Whether or not," says Dr. Rutherford, "the depressing effect on the liver is due to the tendency towards collapse that results from violent purgation, or to the abundant abstraction of certain matters from the portal vein, is doubtful. The point, however, is one of such importance that it demands further investigation.[§]"

In disease.—H. Nasse noted that if his dog became feverish, the amount of bile was decreased.[‖]

Pressure under which the bile is secreted.—Heidenhain, and his pupils, Friedländer and Barisch, found that when a manometer was connected with the gall bladder of a guinea pig, in whom a biliary fistula had been made, the bile or water of the manometer rarely rose above 200 millimeters in height. After reaching this height it remained tolerably constant. The bile is therefore secreted at the small pressure of 200 mm. of water pressure.[¶] Kowalewsky finds that in woorarised cats, the pressure is not constant, but liable to variations, from 12 to 20 mm. of mercury. These variations depend chiefly upon the variations in the arterial pressure. The pressure under which the bile is secreted rises with the rise of the blood pressure. The change is not immediate, but needs some time before it be brought about, due doubtless to some changes going on either in the secretion of the bile or absorption from the ducts. The resistance to the passage of the bile into the bowel also varies in the same species. For example, in woorarised cats it varies from 3·4 to 7·5 mm. of mercury. The bile will thus be stopped entering the duodenum if a resistance of only 3·4 to 7·5 mm. of mercury be opposed to it.*

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[*] Röhrig, Strecker's *Med. Jahrb.* Wien, 1873, p. 248.

[†] H. Nasse, *Commentatio de bilis quotidie, etc.* p. 19.

[‡] Edinburgh Committee, *Report of the Thirty-eighth Meeting of the British Association for the Advancement of Science; held at Norwich, August,* 1868, Lond. 1869, p. 229.

[§] Rutherford and Vignal, *Experiments on the Biliary Secretion of the Dog*, p. 17: Report attached to the *Brit. Med. Journal*, Vol. ii. 1876.

[‖] H. Nasse, *Commentatio de bilis quotidie, etc.* Marburg, 1851, p. 19.

[¶] Friedländer and Barisch, *Arch. f. Anat. Phys.* 1860, p. 659.

Summary of Knowledge as to the Physiology of the Bile. It is much to be regretted that the physiology of the bile is still in so unsatisfactory a state. Compared with it, the chemistry of this humour might almost be looked upon as a well-worked field, although physiological chemistry has made but small progress in what may really be called knowledge.

It is still uncertain if the liver be a mere filter, or if it secrete the bile itself, although the general belief of physiologists is in favour of the latter.

Of late years a belief in a kind of circulation of the bile has much prevailed; that is, that the bile is secreted by the liver, passed into the intestines, absorbed by the intestines, passed into the blood, and again brought back by the blood to the liver to be again excreted.

It is also thought that the bile pigments are direct derivatives of the hæmoglobin of the blood corpuscles, though the evidence in favour of this has of late become weaker. The bile acids must be derived from some nitrogenous bodies, and it is therefore probable enough that they come from the albuminous compounds of the system, though whether the breaking down of the tissues or the splitting up of the peptones from the food furnish the bile acids is not known. It is doubtful if the cholestearin and lecithin be formed in the liver or are merely excreted from the blood. It would appear that a supply of blood from the hepatic artery is needful for the secretion of bile, as, if arterial blood be completely kept out of the liver, death of the liver takes place; but whether the portal vein only bring the materials of the bile is not known.

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* Kowalewsky, *Arch. f. d. ges. Phys.* 1874, Bd. viij. p. 597.

The amount of bile both in man and brutes secreted during the 24 hours is liable to very considerable fluctuations in health. In the few cases in which biliary fistulæ have been established in man, and the amount of bile estimated with care, the bile has varied from 7 to 22 ounces in the 24 hours. In the two instances in which the calculation has been made in man, one kilogramme has secreted 7·34 grm. and 14 grm. of fluid bile, and 0·166 grm. and 0·44 grm. of solid bile in the 24 hours. A glance at the table given by the Edinburgh Committee (see p. 104.) will show how much greater are the variations in dogs.

It would seem likely that the taking of food into the stomach is followed in an hour or two by an increased secretion of bile. In man, it seems doubtful if this be always the case. Perhaps this may be explained by the frequency with which meals are taken by man, by which the liver is being continually excited, and so feels less the stimulus of any one meal; while in dogs, which nature intended should be fed only once in the day, or less often than this, the liver feels the ingestion of a meal as a rare excitement.

During fasting the amount of bile is much decreased.

No definite relation has yet been discovered between the kind and amount of food, and the amount of bile.

During the night, especially after midnight, a less amount of bile is secreted; but it is more concentrated. Observers are much at variance whether drink increase the amount of a diluted bile, as with the urine, or whether it have no influence on the bile, or whether the bile be decreased in amount. Some think that a greater amount of a highly pigmented bile follows the injection of water into the veins.

No nervous influence has yet been found directly to affect the secretion of bile. The diabetic puncture is followed by no change.

On lowering or raising the blood pressure in the liver, the amount of bile which escapes from a biliary fistula is decreased. It is probable that the decrease of bile seen during a low blood-pressure is due to the passing of the bile, already secreted, into the blood, and is not due to a real decrease of secretion.

Purging causes a decrease in the amount of bile secreted.

The bile is secreted in guinea-pigs and in cats at a very low pressure.

Irritation of the papilla in the duodenum, by an acid, is followed by a rush of bile into the duodenum. The acid chyme is therefore probably the natural irritant of the gall-bladder and ducts.

Vomiting is followed by an increased expulsion of bile; so also is muscular exercise.

CHAPTER VII.

THE OFFICE OF THE BILE.

IT would seem necessary that a secretion, which is mixed with the food almost as soon as it leaves the stomach,* which is the product of the largest gland in the body, a secretion in the dog said to equal, in 24 hours, $\frac{1}{50}$ of his weight and of a rabbit $\frac{1}{8}$, should have some notable purpose in the animal œconomy. Yet physiologists have striven, and probably will strive, for many years over the uses of the bile. The same obscurity which hangs over the rest of the physiology of this humour envelopes to an equal, if not a greater, degree, the use to which it is designed by nature.

Is the bile an excrement only or not? It was taught by Aristotle that in animals the gall was an excrement and served no special purpose.† It is said also that Paracelsus considered the bile a useless humour and superfluous member of the animal œconomy.‡ In modern times the doctrine of Aristotle has been maintained, but not wholly, by Tiedemann and Gmelin,§ before Blondlot.

It might be thought this question of the excremental character of the bile would be settled by diverting the natural course of the bile from the intestine to the outside of the body. This was done by Schwann, who devised a method of making such biliary fistulæ. His results were these: out of 18 dogs the common duct was re-established in 2, and in 10 death might be looked upon as the result of the operation. So that only six remain. They died in 7, 13, 17, 25, 64, and 80 days after the operation, with symptoms of inanition, loss of flesh, muscular weakness, unsteadiness of gait, and falling out of the hair. These symptoms were the more pronounced, the longer the animal lived. No difference was seen if the creature licked up the bile from the fistula, or if it were hindered from so doing. Schwann believes that the bile is not solely an excrement like the urine, but is essential to life; that, if it be diverted from the intestine, a loss of weight at once sets in, and that death will follow in 2. or 3. weeks, sometimes more, sometimes less.[*]

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* In omnibus animalibus bilis in principium intestini adfunditur, ut nihil fere alimenti ad sanguinem veniat, quod cum ea non mistum sit. (Haller, *Elem. Phys.* Lugd. Bat. 1764, t. vj. p. 615.)

† Aristotle, *On the parts of animals*, Book iv. Chapter ij. Taylor's ed. Lond. 1810, p. 113.

‡ Paracelsus, quoted by Eisenmann, *Die Krankheits-Familie Cholosis*, Erlangen, 1836, p. 13.

§ Tiedemann and Gmelin, *Recherches &c. sur la Digestion*, Paris, 1827, 2e Partie, p. 58.

Blondlot, on the other hand, set up a biliary fistula in a dog; and after the first week or two, during which the animal was out of health, as it licked the bile from the wound, the dog regained its former state and its usual amount of fat. It ran about the house, and went for walks in the town and country, appearing to ail nothing. Blondlot concludes from this one experiment that the bile is of no use, but is simply an excrement.[†] Schwann later on repeated his experiments on thirty dogs. In the end, all died; but one lived a year, and another four months. Nasse kept a dog alive, with the weight tolerably the same, from the 12th of August in one year, to the 27th of January in the next.[‡] The Edinburgh Committee kept in good health a dog with a biliary fistula

[*] Schwann, *Arch. f. Anat. Phys. u.s.w.* 1844, p. 127.

[†] Blondlot, *Essai sur les Fonctions du foie*, Paris and Nancy, 1846, pp. 55 *et seqq.* This dog of Blondlot's lived five years in perfect health, was active, used for hunting, and had pups every year. It died without apparent cause, and on dissection the obstruction of the ducts was found to be perfect. (See *Comptes rendus*, 1851, t. xxxii. p. 904.)

[‡] Schwann and Nasse, quoted by Frerichs, Wagner's *Handwörterbuch d. Physiologie*, Braunschweig, 1846, Bd. iii. Abth. i. p. 837.

from April 24, 1868, to September 11 of the same year. It gained nearly 4 kilogrammes in weight during the five months that it lived without bile passing into the intestine; and had kept its strength, notwithstanding a partial poisoning with corrosive sublimate, purging with podophyllin, and dosing with taraxacum.* The Committee think that much depends on the health of the animal at the time that the biliary fistula is established. If the strength be good, health is usually preserved.

The observations of Bidder and Schmidt confirmed in all the more important particulars the results of Schwann. In their first experiment they found the dog to lose weight daily, although he was fed with four hundred grammes (nearly half a pound) of meat. His weight before the operation was six kilogrammes; after death at the end of a month, less than three and a half. Thus, the wasting of the animal was something very noteworthy. The skin was loose, the muscles scarcely to be felt, and the movements of the animal were very weak, although it was only on the day before its death that it did not leave its kennel. The hairs fell out in great abundance, leaving bald spots on the trunk and limbs. A great contrast to the miserable appearance, was the enormous appetite, of the creature. Digestion seemed to go on much as usual. The stools were not frequent, but were remarkable for their filthy smell; so also was the flatus which was passed by the animal almost incessantly. Much the same appearances were seen in their second experiment. In their third, the spleen was first removed and then a fistula set up. The dog lived two months and was killed. It showed the same great appetite, loss of flesh, and other symptoms that the others did; only it seemed to preserve its health.

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* Edinburgh Committee, *Report of the Thirty-eighth Meeting of the British Association for the Advancement of Science; held at Norwich in August*, 1868, London, 1869, p. 231.

Bidder and Schmidt conclude that the question whether the bile be merely an excretion cannot be answered simply with yes or no.[*] In some cases it may be looked on as such, when the drain caused by the loss of bile can be fully covered by the increased amount of food taken; but in the greater number this compensation is not possible, and the loss becomes so great that life can no longer be kept up.

Is the bile needful for digestion in the stomach and intestines? Eaglesfield Smith found some advantage to the digestion in a case of jaundice in administering the bile of mammals. In Abyssinia and other uncivilised countries, he says, bile is thought to be a stomachic and a luxury;[†] he immersed flesh in gall for 14 hours at a heat equal to the human body, and found that it had lost half its weight; and he thinks therefore that bile is of great aid in digestion, due to its power of acting on grease.[‡]

In order to test this theory that the bile aided the formation of chyle, the first Sir Benjamin Brodie conceived the idea of tying the bile duct, and thus hindering the bile from passing into the intestine. He then watched the effect on the digestion. That in the stomach he found to continue as usual; but the conversion of chyme into chyle was invariably and completely interrupted: not the smallest trace of chyle was perceptible either in the intestines or in the lacteals.[§]

Magendie repeated Brodie's experiments in two animals, and found that white chyle was formed, together with fæces which resembled ordinary fæces save that they were white.[*] Tiedemann and Gmelin, however, found that while the liquid in the lacteals of dogs whose bile ducts had not been tied was whitish, it was without colour and clear in those in whom they had been tied; so also was the fluid in the thoracic duct. The difference is due to the absence of fatty particles which give a milky appearance to the fluid. The formation of chyle was not absolutely put an end to, as Brodie maintains, but that less fat was absorbed when the bile was hindered from passing into the duodenum.[†]

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[*] Bidder and Schmidt, *Die Verdauungssaefte*, Mitau and Leipzig, 1852, pp. 98-114.

[†] Dr. George Harley says that bile is drunk with great glee by the Kaffres. (*Jaundice*, London, 1863, p. 18.)

[‡] Eaglesfield Smith, *European Magazine*, 1797, Vol. xxxi. p. 386. Cf. *Observations and experiments on the digestive powers of the bile in animals*, Lond. 1805.

[§] Brodie, *Quarterly Journal of Science*, 1823, Vol. xiv. p. 342.

Bidder and Schmidt examined the chyle from the thoracic duct of dogs with biliary fistulæ; in no case did they find it white, but opalescent, transparent, now and then yellowish; it clotted as soon as taken from the duct. Of three cases, there were 55·26, 58·42, and 83·38 *pro mille* of solids, figures which are within the averages of health. The amount of fat in the chyle was, however, very small. The amount with ordinary nourishment in a healthy dog may be as high as 32 *pro mille*. In these it was under 2 *pro mille*.

Bidder and Schmidt also examined the fæces of animals in whom the bile was cut off from the intestine. They found that the albuminous bodies of the food had almost entirely disappeared from the fæces; so also had the starch, while a good part of the fats was also absorbed; one kilogramme of the animal taking 5·17 grm. of fat in the 24 hours.[‡] Some part of the fat which is ordinarily absorbed is therefore not taken up when bile is not present.

Certain Chemical Properties of the Bile. These properties should have been discussed under the chapter on the chemistry of the bile; but it is more convenient to consider them at this point with the use of the bile in the digestion of aliments.

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[*] Magendie, *Précis élém. de phys.* Paris, 1836, 4e éd. t. ij. p. 119, note.

[†] Tiedemann and Gmelin, *Recherches exp. etc. sur la Digestion*, Paris, 1827, 2e Partie, pp. 55 and 95.

[‡] Bidder and Schmidt, *Die Verdauungssaefte*, Mitau and Leipzig, 1852, pp. 270-228.

That bile has some power of emulsifying fats is well known from its domestic use. When shaken up with oil it forms an emulsion better than plain water, but not nearly so well as pancreatic juice. Dr. Bence Jones says that bile has no chemical action whatever on the neutral fats.[*] And in this Lenz[†] and others agree with him. Lenz says that if ox bile be mixed with an equal quantity of pure oleic acid, shaken together, and the whole kept at a temperature of 35° to 40° C. (95° to 104° F.) then three layers are formed; the uppermost contains pure oleic acid; the lowest pure bile; while the middle is of a whitish green colour and soluble in water. This can be again divided by hydrochloric acid into two layers, one of pure oleic acid, the other of chloride of sodium. So that it is the soda salts of the bile which form a soap with the fatty acids. Free fatty acids may be formed by the action of the pancreatic juice. But the greater part of the fat of the chyle is not soap, but finely-divided fat in minute drops and granules.

C. A. von Wistinghausen found that oil passed more readily through animal membranes moistened with bile than with water; and more readily at the temperature of the body than at a temperature of 19° C. Also that oil rose more readily in capillary tubes wetted with bile than in tubes that were dry or wetted with water.[‡]

Mr. Charles H. Williams has also made some careful investigations on this point in Professor Bowditch's laboratory in the Harvard Medical School. He finds that oils pass more readily through membrane or plaster wet with bile than through membrane or plaster wet with water. This is increased if the bile be alkaline and decreased if it be acid.

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[*] Bence Jones, *Medical Times*, 1851, July 5, p. 3.

[†] Lenz, *de adipis concoctione et absorptione*, diss. inaug. Dorpati, 1850, quoted by Bidder and Schmidt, *op. cit.* p. 228.

[‡] C. A. von Wistinghausen, *Experimenta quaedam endosmotica de bilis in absorptione adipum neutralium partibus*, Diss. Inaug. Dorpati Livonorum, 1851. This tract, which had been almost forgotten by physiologists, has been reprinted in substance by J. Steiner, in *Archiv f. Anat. Phys. u.s.w.* 1873, p. 137.

He concludes that the action cannot be due to the bile changing the form of the pores; and he finds also that after passing through membranes moistened with bile, the fats appear more finely divided than when passed through membranes wet with other fluids; and he infers that the drop-tension or cohesion of the fat has been affected.[*]

Thirty years ago it was denied that bile had the property of turning starch into sugar; but von Wittich has shown that this office is enjoyed by fresh human bile as well as that of many animals.[†] Bufalini has of late confirmed this observation of von Wittich's, and further finds that fresh bile has also the property of changing the hepatic glycogen into sugar. When bile is deprived of its mucus and pigments by means of slight acidulation with acetic acid and animal charcoal, it still retains this power; but the change is longer in being accomplished, probably because some of the ferment is carried away with the mucus. Putrefying bile does not change starch or glycogen into sugar; nor do the bile acid salts.[‡]

Upon the sugars themselves bile appears to have no more action than other animal matters have. Thus it forms lactic acid if kept for a long time with

[*] Charles H. Williams, *Experiments on the action of Bile in promoting the absorption of Fats*, Prize Essay of the Boylston Medical Society for 1874, published as Supplement to the ninetieth volume of the *Boston Medical and Surgical Journal*.

[†] von Wittich, *Arch. f. d. ges. Phys.* 1872, Bd. vj. p. 182. H. Hoffman (Häser's *Archiv* 1844, Bd. vj. p. 157, Bericht in *Arch. f. Anat. Phys. u.s.w.* 1846, p. 27) distinctly says that bile can turn starch (Kleister) into dextrin and sugar.

[‡] Bufalini, *Lo Sperimentale*, abstract in *London Medical Record*, 1879, p. 149.

grape sugar or cane sugar.[*] It was once thought that bile could turn sugar into fat;[†] a notion refuted by the experiments of Schiel,[‡] and Frerichs.[§]

Bile has no solvent action on the albumens. Hünefeld noticed that the bile dissolved the red blood corpuscles[‖] and this property was extended to the more important articles of diet, so that Platner allowed a certain small power in bile to dissolve loosely-clotted albumen, fibrin, and casein.[¶] The experiments of von Gorup-Besanez[**] showed that bile had no influence on white of egg, boiled or fresh beef, but seemed to favour the idea that cheese was dissolved by bile. This has been disproved by the experiments of Bidder and Schmidt.[††]

A strange view of the office of the bile was entertained by Prout. "If the food originally contained no albuminous matter; no albumen is developed in the stomach; but immediately on the entrance of the semi-fluid mass into the duodenum, and its mixture with the bile and the pancreatic fluids; albuminous and other chylous matters, become distinctly perceptible." Later on he says that some of the albumen may be developed from the pancreatic fluid, but the whole is too great to be explained in this manner.[‡‡]

It was known early in this century that the chyme was thrown down when brought into contact with bile.* It was also demonstrated by Eberle† and insisted on by nearly every physiologist after him. Platner apparently believed that the precipitate was a combination of the bile acids with albumen or pepsin.‡ He stated that the combination of bile acids and albumen could hardly be digested even if kept for days with artificial gastric juice.

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[*] Bence Jones, *Medical Times*, 1851, July 5, p. 3. This is probably copied from Frerichs, who says the same thing. (Wagner's *Handwörterbuch d. Physiologie*, Branschweig, 1846, Bd. iii. Abth. i. p. 835.)

[†] Henr. Meckel ab Hemsbach *de genesi adipis in animalibus* Diss. inaug. med. Halis; quoted in Canstatt's *Jahresb. f.* 1845, Bd. i. p. 145.

[‡] Schiel, *Zeitschrift f. rat. Med.* 1846, Bd. iv. p. 375.

[§] Frerichs, *loc. cit.*

[‖] Hünefeld, *Der Chemismus in der thierischen Organisation*, Leipzig, 1840, p. 102.

[¶] Platner, *Ueber die Natur u.d. Nutzen d. Galle*, Heidelberg, 1845, p. 124.

[**] E. von Gorup-Besanez, *Untersuchungen ueber Galle*, Erlangen, 1846, p. 46.

[††] Bidder and Schmidt, *op. cit.* p. 219.

[‡‡] Prout, *Chemistry, Meteorology, and the Function of Digestion considered with reference to natural Theology*, Bridgewater Treatise, London, 1834, p. 508.

It was very distinctly taught by Claude Bernard that if bile be added to the gastric juice, the work of digestion is at once arrested. If meat be kept in gastric juice at the proper temperature, the particles of the muscular fibres are broken up, and this is the peculiar office of the gastric juice. But if bile be added, the process ceases at once. The presence of bile in the stomach puts an end to digestion. Even if the gastric juice remain acid, it loses its digestive properties.

When the albuminous bodies which have been dissolved by the gastric juice arrive in the duodenum, they are at once thrown down by the bile; but the bodies free from nitrogen remain untouched. No precipitate is formed if bile be added to the gastric juice from a fasting animal, or from one which has eaten only fat, starch, or sugar. But when the nitrogenous elements of the food pass through the pylorus, a yellow precipitate is thrown down of everything dissolved, and this precipitate adheres to the walls of the gut. The viscid secretion of the duodenal glands helps to entangle the precipitate, and to keep it in the duodenum, to undergo for a longer time the action of the digestive fluids.

By the precipitation of the chyme by the bile, the activity of the gastric juice is wholly brought to an end. If the chyme be filtered, the filtrate has no longer any digestive power.[*]

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* Autenrieth, *Handbuch d. emp. mensch. Physiologie*, Tüb. 1802. Bd. ij. p. 98. Werner, quoted by Eberle, *Physiologie der Verdauung*, Würzburg, 1834. p. 210. Blundell, 1817, quoted by Elliotson, *Human Physiology*, London, 1840. p. 101, note.

† Eberle, *Physiologie d. Verdauung*, Würzburg, 1834, p. 190.

‡ Platner, *Ueber die Natur und den Nutzen der Galle*, Heidelberg, 1845, p. 126.

That the gastric juice holding peptones in solution is thrown down, and rendered inactive, by the addition of bile, is assented to by nearly every physiologist. Dr. Dalton, however, says that he has invariably found that if the gastric juice be digested with white of egg, the filtered fluid will no longer give the slightest precipitate on the addition of bile.[†]

According to Claude Bernard, the precipitate thrown down by the bile from the chyme is redissolved by the pancreatic juice. Also if pieces of the food, such as casein or flesh, not yet entirely dissolved by the gastric juice, be acted on by bile, digestion begins anew as soon as the pancreatic juice is added. This renewal of digestion does not take place unless the chyme have first been subjected to the interruption of digestion by the bile; so the interruption by the bile seems needful to render the pancreatic juice active, and the order of succession would be (i.) gastric juice (ii.) bile (iii.) pancreatic juice.[‡] This is somewhat in opposition to the experience of physiologists who find that digestion goes on much the same in the intestines after tying the common duct; and especially to those experiments of Bidder and Schmidt who found all the elements of the food well digested, save only the fats and oils.[§]

Tiedemann and Gmelin,[‖] Frerichs,[¶] and an observer so late as Lucien Corvisart,[**] taught that it was not the albuminous parts of the chyme that were thrown down by contact with the bile, but the mucus and colouring matters of the bile itself. Brücke has tried to disprove this by removing the mucus of the bile by rendering the bile acid with phosphoric acid, filtering, and then adding the filtrate to chyme; there is thrown down an abundant white precipitate, composed of peptones.[*] Schiff criticises this, for he says that although Brücke's statements are true, yet his interpretation is false. They prove nothing about the physiological action of the bile upon the chyme. Schiff finds that it is only when the bile is rendered more acid than the gastric juice, that a precipitate of peptones is thrown down. He does not, however, deny that bile throws down peptones. Indeed, he recommends this humour as a substitute for Millon's reagent in ascertaining the presence of albuminates not thrown down by heat.[†]

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[*] Claude Bernard, *Leçons de Physiologie exp.* Paris, 1856, t. ij. p. 421.

[†] John C. Dalton, *A Treatise on Human Physiology*, Philadelphia, 1871, Fifth ed. p. 180.

[‡] Claude Bernard, *op. cit.* t. ij. p. 441. See the observations of Heidenhain on the pancreatic juice and bile below. (p. 143.)

[§] See above, p. 136.

[‖] Tiedemann and Gmelin, *Recherches expérimentales, etc. sur la digestion*, Jourdan's transl. Paris, 1827, Partie ii. p. 395.

[¶] Frerichs, Wagner's *Handw. d. Phys.* Braunschweig, 1846, Bd. iii. Abth. i. p. 834.

[**] Lucien Corvisart, *Comptes rendus*, 1857, t. xliv. p. 720.

According to Burkart the bile has a very distinct action upon the gastric juice. A precipitate is thrown down which on examination is found to be a mixture of the pepsin of the gastric juice with the bile acid, and the supernatant fluid is devoid of any digestive power.[‡] This precipitation Burkart thinks is due to the presence of glycocholic acid in the bile, not to taurocholic acid.[§] The acid of the gastric juice separates the glycocholic acid from its base and this acid is thrown down with the pepsin mechanically adhering.

Hammarsten finds that the digestive power of the gastric juice is destroyed by the bile of many species of mammals, and also of birds and fishes. He thinks it may be a common property of the bile of all vertebrate animals.

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[*] Brücke, Moleschott's *Untersuchungen zur Naturlehre*, Giessen, 1862, Bd. viii. p. 335.

[†] M. Schiff, *Arch. f. d. ges. Phys.* 1870, Bd. iii. p. 620.

[‡] Burkart, *ibid.* 1868, Bd. i. p. 208.

[§] Idem, *ibid.* 1869, Bd. ii. p. 182.

He further finds that a precipitate is not always formed by the addition of bile to the gastric juice,[*] but only when the gastric juice contains albumen; and that the digestive power of the gastric juice may be taken away even while the fluid remains quite clear. The pepsin, however, is not decomposed by the bile acids, for it can be found again. Cubes of hard-boiled white of egg or shreds of fibrin are not acted on at all by gastric juice, if they be kept beforehand for a few hours in a mixture of gastric juice and bile, or of hydrochloric acid and bile. This is due to some union between the bile and the albumen; for he found in the experiments just mentioned that the amount of solids in the gastric juice always decreased, while the weight of the cubes of hard-boiled white of egg increased. Apparently there is a chemical union between the bile acids and the albumen.

He finds also that glycocholic acid is less active than bile itself, and that taurocholic acid is more active than glycocholic acid in destroying the digestive properties of the gastric juice. In this matter he is in direct contradiction with Burkart. He thinks it possible also that the other elements of the bile may have some share in destroying the power of pepsin; but as no means are known of dissolving cholestearin or the pigments but by agents which would at the same time greatly disturb digestion, the question at present cannot be settled.[†]

In contrast to the action of bile upon gastric juice, Heidenhain found that when bile is added to pancreatic juice in action, the process is not put a stop to, but is rather favoured.[‡]

According to Hoppe-Seyler's observations, the pancreatic juice does not seem to split up the bile acids into cholalic acid, taurin, and glycocoll, with any very great rapidity.[*]

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[*] This exactly agrees with the statement of Claude Bernard, who found that no precipitate followed the addition of bile to the gastric juice from an animal fasting. (*Leçons de Physiologie exp.* Paris, 1856, t. ii. p. 422.)

[†] O. Hammarsten, *Arch. f. d. ges. Phys.* 1870, Bd. iii. p. 53.

[‡] Heidenhain, *ibid.* 1875, Bd. x. p. 579.

I have not met with any direct experiments as to the action of the bile upon the *succus entericus*, but the bile is also said to stimulate the secretion of the intestinal juice, and to increase the peristaltic movements.[†] In favour of this, Tiedemann and Gmelin found that the fæces of animals whose bile ducts had been tied were very firm, and that the dogs were costive.[‡] The same thing has been noted in dogs in whom a biliary fistula has been set up.[§]

Eberle found that the bile acted on the bowels as an irritant, increasing their movements, and causing an abundant secretion from the mucous membrane;[‖] and Schülein has lately said that the administration of the bile acids, whether by the mouth or by the veins, is followed by purging and vomiting; and that cholalic acid is more active in this way than glycocholic or taurocholic acid. He thus thinks it likely that the bile may increase the peristaltic movements of the intestines,[¶] as Eberle has suggested.

Another use of the bile was formerly thought to be the neutralisation of the acid of the gastric juice;[**] but as the bile is commonly neutral in reaction, and but rarely alkaline, it is clear that this cannot be its chief office. This view prevailed longer than natural; for it was adopted by C. H. Schultz in his theories on the amount of the bile, and these again were brought into prominence by Liebig.[*]

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[*] Hoppe-Seyler, *Arch. f. path. Anat.* 1863, Bd. xxvi. p. 532.

[†] Saunders thought this to be its principal office. (*A Treatise on the Structure, Economy, and Diseases of the Liver*, Lond. 1803, Third ed. p. 151.) and Sir Thomas Browne (*Pseudodoxia Epidemica* or *Enquiries into Vulgar and Common Errors*, Book iii. Chapter ii. London, 1650. Sec. Ed. page 88.) expresses the common belief of the 17th and 18th centuries when he says: Choler is the naturall glister, or one excretion whereby nature excludeth another; which descending daily into the bowels, extimulates those parts, and excites them unto expulsion. And therefore when this humour aboundeth or corrupteth, there succeeds oft times a *cholerica passio;* that is, a sudden and vehement purgation upward and downward.

[‡] Tiedemann and Gmelin, *op. cit.* Partie ii. pp. 47 and 70.

[§] Schwann, Bidder and Schmidt, *ll. citt.*

[‖] Eberle, *Physiologie der Verdauung*, Würzburg, 1834, p. 314.

[¶] M. Schülein, *Zeitschrift f. Biologie*, 1877, Bd. xiii. p. 172.

[**] Boerhaave is said by Tiedemann and Gmelin to have been a supporter of this theory. (Tiedemann and Gmelin, *op. cit.* Partie i. p. 384.) I can hardly think

The bile is thought to hinder putrefaction. Bidder and Schmidt,[†] with other observers, noted the disgusting smell of the fæces and flatus of dogs in whom the bile had been diverted from the intestines. The same thing is said to be seen in jaundice, though I can hardly assent myself to this as a general rule. The bad smell is attributed to the lack of the antiseptic action of the bile. Saunders attributed the antiseptic powers of bile to its bitterness, and found by experiment that bile became putrid less readily than blood.[‡] Von Gorup Besanez thinks the antiseptic powers of the bile due to the bile acids. He put meat and albumen into a solution of the bile acids, and kept the mixture for 48 hours at the temperature of the body. At the end of this time there was no trace of putrefaction; while meat and albumen put into plain water and treated in the same way gave distinct signs of putrefaction at the

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that Boerhaave was of opinion that the bile had an alkaline reaction. Speaking of the properties of the cystic bile, he says: "nec alcalica est, nec acida." (*Opera Omnia Medica*, Venetiis, 1757, p. 20. Institutiones Medicæ, § 99.) On the other hand he says a little later on: (p. 22 § 107) " Bilis Alcalina acidum Chylum fixum in salsum volatile Alcalescens immutans; Pancreaticæ Lymphæ acor et cum bile Alcalina fervor; . . . . et innumeræ tales hypotheses, damnosæ, dum, regulas dant faciundæ Medicinæ."

Kemp (*Lond. Med. Gaz.* 1845, vol. i. p. 77.) says he has examined 200 samples of bile and found them all neutral.

[*] See p. 94 of this work.

[†] Bidder and Schmidt, *op. cit.* p. 104.

H. Hoffmann is said to have an important paper on the antiseptic powers of the bile, (Häser's *Archiv* 1844, Bd. vi. p. 157.) but I have not been able to see a copy of this in London.

[‡] Saunders, *op. cit.* pp. 136 and 155.

end of 24 hours.* He found also that fermentation set in much later when bile was mixed with syrup, urine, and the like, than without. This experiment has been confirmed by Claude Bernard, who found that bile at once checked the fermentation of yeast from the stomach of a dog.†

More lately Stolnikoff has made a few experiments in Hoppe-Seyler's laboratory at Strassburg on this point. Bile and water; fibrin, bile, and water; fibrin, fat, and water; and fibrin, fat, bile, and water were left in bottles from the middle of June to the middle of August, and the gases given out collected over mercury. The bile simply mixed with water had given out no gas; but the mixture of fibrin and fat without bile had given out most of all. The gas showed 92 *per cent.* of carbonic acid. The contents of the bottles showed the bile acids split up into cholalic acid, taurin, and glycocoll, as might have been looked for. Stolnikoff concludes that bile is able for a short time to delay putrefaction, but not to hinder it altogether, as the bile and water itself had split up into new products, although no gas had been given off. Stolnikoff does not think that the office of the bile is to stop putrefaction in the intestines, but rather to favour absorption.‡

Haller thought that the use of the bile was to aid in the solution of the food, and to form one homogeneous mass with mucus, oil, and water, by trituration and the peristaltic action of the bowels.§

Changes of the bile in the intestines.—After the bile has been poured into the duodenum, and done whatever it is appointed to do, whether it be a positive harm to the process of digestion, a suggestion which in the present state of knowledge may perhaps be entertained; or be simply an indifferent fluid; or in some way aid the pancreatic juice; what becomes of the humour? Does it pass entirely out of the body with the fæces, or is it absorbed again into the circulation?

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* E. von Gorup-Besanez, *Untersuchungen ueber Galle*, Erlangen, 1846, pp. 48 and 50. The first of these experiments was made with the same result by Platner. (*Ueber die Natur und den Nutzen der Galle*, Heidelberg, 1845, p. 128.)

† Claude Bernard, reported by Donaldson, *American Journal of the Medical Sciences*, 1851. Vol. xxii. p. 351.

‡ J. Stolnikoff, *Zeitschrift f. phys. Chemie*, 1878, Bd. i. p. 343.

§ Haller, *Elem. Phys.* Lugd. Bat. 1764, t. vi. p. 608.

Liebig and his followers assumed that the greater part of the bile was absorbed to aid in the combustion of respiration.[*] Mulder, on the other hand, taught that the greater part of the bile was passed out by the anus,[†] while Frerichs held that neither of these views was wholly correct,[‡] at the same time stating that of the bile only a small part was absorbed.

Bidder and Schmidt, in order to settle this question, estimated the amount of bile in the fæces passed in five days by a dog weighing 8 kilogrammes. The fæces weighed 97·3 grm. of which 40·9 grammes were solid. Now the solids of the bile passed in five days would be 39·52 grm. that is nearly equal to the solids of the fæces; yet the fæces showed but small traces of the presence of bile. Still more important was the amount of sulphur in the fæces. The bile of dogs holds about 6 *per cent.* of sulphur: so that in 39·52 grm. of solid bile, there should be nearly 2·37 grm. of sulphur. As a fact, the fæces only held 0·334 grm. of sulphur; and without doubt more than half of this came from the numerous hairs in which the fæces abounded.[§]

It was said by Frerichs in 1846 that as soon as the bile entered the intestine, the bile acids broke up into taurin, chloidic acid, and dyslysin, and that in the end only dyslysin could be detected. The pigment is described as passing from green into brown, and at last attaining the characters of the colouring matter of some gall stones.[*] The cholestearin at this time seems to have been neglected.

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[*] Liebig, *Animal Chemistry*, London, 1842, Gregory's translation, Sec. Ed. pp. 60-66.

[†] Mulder, *Untersuchungen über die Galle*, Frankf. a. M. 1847, p. 107. He teaches that the bile begins to decompose as soon as it is secreted.

[‡] Frerichs, in Wagner's *Handwörterbuch d. Physiologie*, Braunschweig, 1846, Bd. iii. Abth. i. p. 839.

[§] Bidder and Schmidt, *op. cit.* p. 217.

But in 1862 Hoppe discovered the presence of free cholalic acid in the fæces of dogs,[†] and in a few months the same observer announced that, as well as cholalic acid in quantity, he found undecomposed glycocholic and taurocholic acid in the fæces of dogs and cows, and certain elements of the bile in the fæces of pigeons, and in guano from Peru. He estimated the amount of cholalic acid in the fæces of a dog weighing 8 kilogrammes and fed on beef. The weight of the fæces for three days was 287 grammes, and the amount of cholalic acid was 1·1 grm. estimated by the polariscope. This equals ·36 grm of cholalic acid a day, or ·45 grm. of taurocholic acid. Now taking Bidder and Schmidt's estimate for the amount of solids in the bile excreted by a dog of this weight as 8 grm. in 24 hours,[‡] and one half of this as made up of bile acids, there will be at the most only half a gramme out of 4 grammes of bile acids accounted for in the fæces. What becomes then of the remaining three and a half grammes?

Hoppe-Seyler analysed the contents of different parts of the intestines of dogs and rabbits, and found that though the splitting up of the taurocholic acid began in the small intestine, yet it chiefly progressed in the large intestine. He thinks it a spontaneous change; for none of the secretions poured into the intestine contains a ferment capable of setting the change in motion: also that the change is quite analogous to that of the splitting up of hippuric acid, and notes that the fæces of dogs hold a quantity of free butyric acid, valerianic acid, caproic and caprylic acid, products of decomposition in the large intestine.*

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[*] Frerichs, in Wagner's *Handwörterbuch d. Physiologie*, Braunschweig, 1846, Bd. iii. Abth. i. pp. 840 and 841.

[†] Hoppe, *Archiv. f. path. Anat.* 1862, Bd. xxv. p. 181.

[‡] See p. 100 of this work.

It will have been seen above that Hoppe-Seyler and his followers assert that the bile acids become decomposed in the intestines into taurin and glycocoll, with the formation of free cholalic acid. Uncombined taurin and glycocoll are not found in the fæces, so it is probable that they, or the products of their decomposition, are absorbed again into the blood. Schultzen and Nencki, in their admirable research into the decompositions which lead to urea, found that when an animal, the amount of urea in whose urine was constant, was fed with glycocoll, the urea was at once increased to an amount equivalent to the amount of glycocoll ingested. Glycocoll, therefore, on its way through the œconomy becomes changed into urea, and in this way leaves the body.† Taurin would also seem to pass out of the body by the urine, as Salkowski found that in man taurin given by the mouth again appeared in the urine, partly as unchanged taurin, but in great part as an acid containing sulphur and nitrogen (taurocarbamic acid) the normal sulphates not being increased.‡

If some of Ernst Bischoff's estimations were accepted as representing a general rule, there might be no need of discussing further the fate of the bile in the intestines. He found the fæces rich in bile, about 10 *per cent.* of unaltered bile acids, while the cholalic and choloidic acids were not more than 1 *per cent.* Altogether he thinks that man passes daily *per anum* about 5 grammes of solid bile.[*] Now 5 grammes of solid bile would be about the amount secreted daily by the liver in the cases of biliary fistula in man observed by Dr. Robinson and Krumptmann,[†] and Leyden adopts 2 to 4 grammes as the amount of bile acids daily secreted by the liver.[‡] Calculations of this sort must not be pressed too far, as there appear to be as great variations in the amount of bile secreted by man as by any other animal.

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* Hoppe-Seyler, *ibid.* 1863, Bd. xxvi. p. 519.

† Schultzen and Nencki, *Zeitschrift f. Biologie*, 1872, Bd. viii. p. 132.

‡ Salkowski, *Berichte der deutschen chem. Gesellschaft zu Berlin*, 1872, Jahrg. v. p. 637. See also an abstract by himself in Virchow and Hirsch's *Jahresbericht f.* 1873, Bd. i. p. 159.

In 1869, Schiff announced that the bile acids and bile pigments are again absorbed into the portal circulation and again excreted by the liver. In a dog, upon whom a biliary fistula had been made, the amount of bile excreted was about 2 C.C. in 20 minutes. If 180 C.C. of fresh ox bile were now injected into the duodenum, a surprising increase of the amount of bile took place; so that in a very short time 10 C.C. of bile could be collected in 20 minutes from the fistula, and at the end of an hour 8·5 C.C. in 20 minutes. Schiff then availed himself of a statement of Heidenhain's, that the bile of the guinea-pig gives no reaction with Pettenkofer's test. He established a fistula on a guinea-pig, and found no decided reaction in the bile when tested by Pettenkofer's test; ox bile was then injected into the duodenum, and in half an hour, and up to 1, 2, or 3 hours after, the bile gave a marked reaction with Pettenkofer's test, just as if ox bile had been diluted with 2 or 3 times its volume of water. As to the pigments, the natural colour of the bile of dogs is a golden yellow; when ox bile was introduced into the duodenum of dogs, the bile became dark and brown.

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[*] Ernst Bischoff, *Zeitschrift f. rat. Med.* 1864, Bd. xxi. p. 143.

[†] See p. 97 of this work.

[‡] Leyden, *Beiträge zur Pathologie des Icterus*, Berlin, 1866, p. 55.

The phænomena prove in Schiff's opinion that there is a circulation of the bile, as well as of the blood; that the bile is poured out by the liver into the intestine, there again to be taken up by the mesenteric vessels, carried to the liver, and again excreted into the duodenum.[*] In another article, he repeats his belief that the secretion of bile is almost wholly dependent on absorption from the intestine, and that if the bile be cut off from the intestine, little or no bile is secreted.[†]

Theodor Laffter, under Heidenhain's direction, has repeated Schiff's experiments, and differs from him considerably in his results. When ox bile was injected into the duodenum of guinea pigs, a very slight increase of the amount of bile was seen in some, in others a decrease. Laffter does not attribute this decrease to the action of the bile, but to a peculiarity of the animal. Laffter agrees with Schiff in announcing an increase in the solid bile, but the amount seems to me so small that it may easily be within the boundaries of physiological variation. In one matter Laffter has made a curious observation; he finds that colouring matters, such as rhubarb and indigo-sulphate of soda, injected into the duodenum, very rapidly appear in the bile; in one reading of the text, Laffter may be thought to say within a minute after the injection into the duodenum.[‡]

Following upon Laffter, Prince Tarchanoff entered upon a research to show that the liver has also the power of rapidly excreting other colouring matters. If blood colouring matter or bilirubin be injected into the veins of a dog with a biliary fistula, a great increase of the water and pigments of the bile follows.[§]

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[*] M. Schiff, *Giorn. di Scienze Naturali ed Econ.* Palermo, 1869, vol. iv. p. 9.

[†] M. Schiff, *Arch. f. d. ges. Phys.* 1870, Bd. iii. p. 598.

[‡] Theodor Laffter, *Versuche zur Physiologie der Gallensecretion*, Diss. Inaug. Breslau, 1873. It is not so clearly expressed as I could wish that this last colouring matter was injected into the duodenum. I am indebted to Dr. Lauder Brunton for the opportunity of seeing the original dissertation.

[§] Johannes, Fürst Tarchanoff, *Arch. f. d. ges. Phys.* 1874, Bd. ix. p. 329.

Huppert's observations are generally quoted as if they gave aid to Schiff's belief that the bile acids are excreted by the liver. He injected a certain quantity of bile acids into the circulation of a rabbit in whom a biliary fistula had been set up, and found that the liver excreted about the fourth to the third part of the bile acids injected.[*]

Socoloff has repeated, in Hoppe-Seyler's laboratory, some experiments like those of Schiff, but he has not obtained precisely the same results. After the injection of the glycocholate of soda into the veins or stomach of dogs, he found indeed that there was an increase, very marked, of the amount of bile secreted. And this increase took place, as Schiff found it, within 15 minutes after the injection. With this increase of the bile itself, there was always a marked decrease of the amount of bile acid salts. There was not the least increase of the solids of the bile. Now if this be maintained, a blow will certainly be dealt to the views of Schiff and his followers, as Schiff himself expressly states that there is an increase in the amount of the solids of the bile.[†]

Socoloff notes also that in Huppert's experiments the increase of bile after the injection of bile acids was first noted in the second hour, just as Bidder and Schmidt did in their experiments without injection. He criticises justly also Schiff's observations on guinea pigs, noting that Pettenkofer's test is not enough alone to enable a man to assert the presence of bile acids, but that the bile acids should be crystallised out, as Socoloff has done.[‡]

It may be noted also that Laffter[§] and Külz[‖] deny the statement of Schiff that the bile of guinea pigs gives no reaction with Pettenkofer's test. And it must be owned that it does seem highly improbable that the bile of a vertebrate should be without evidence of the presence of bile acids.

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[*] Huppert, *Archiv der Heilkunde*, 1864, p. 244.

[†] Schiff, *Arch. f. d. ges. Phys.* 1870, Bd. iii. p. 599.

[‡] Socoloff, *ibid.* 1875, Bd. xi. p. 166.

[§] Laffter, *op. cit.* p. 11. Work done in Heidenhain's laboratory.

[‖] Külz, Virchow and Hirsch's *Jahresbericht f.* 1875, Bd. i. p. 219.

Tappeiner has also made estimations on the absorption of bile acids by the small intestine. Dogs were fasted for 24 hours, and then a certain quantity of dog's bile, or a solution of glycocholate of soda, injected into a tied-off part of the small intestine. After the bile acid salt or the gall had been left in the bowel from 3 to 5 hours, the amount of bile acids and of sulphur was estimated. In the upper part of the small intestine, the duodenum and jejunum, the whole of the sulphur of the bile was found again; in the ileum, never more than one third. Of glycocholate of soda none was absorbed in the duodenum; but in the jejunum and ileum, never more than one half could again be found.

Tappeiner refuses to admit a chemical change as the cause of a decrease in the amount of bile acids found. The first step in a chemical change would be the decomposition of the bile acids into cholalic acid, taurin, and glycocoll. Now it was found that taurin is readily absorbed by the intestines of dogs; but when taurocholic acid was injected into the jejunum, the whole quantity injected was found again.* It may be admitted that there is no decomposition in the parts of the intestines where the amount of bile acids injected was again recovered, but this will hardly be allowed to hold good for the ileum, where only one half or one third of the bile acids could again be recovered, and which may therefore have undergone the decomposition in question before they were absorbed.

Amongst the older authors, Tiedemann and Gmelin found cholestearin in the contents of the small intestine of certain mammals, and in the large intestine of the calf.[*] But Dr. Austin Flint, the younger, is of opinion that no cholestearin can be found in normal fæces, only a product of the decomposition of cholestearin, named serolin by Boudet, but which Dr. Flint calls stercorin.[†] The elimination of cholestearin he looks upon as a most important office of the liver. Hoppe-Seyler, commenting upon the observations of Dr. Austin Flint, says that he has always found cholestearin in the fæces of dogs, oxen and men ; and he does not doubt that Dr. Flint's stercorin and Boudet's serolin are but impure cholestearin.[‡] Dr. Flint's theory would in this case fall to the ground, if Hoppe-Seyler's facts be accepted ; and I think that evidence offered by this distinguished chemist on a matter like the finding of cholestearin will be hard to be overturned.

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* Tappeiner, in von Buhl's *Mitt. aus d. path. Inst. zu München*, Stuttgart, 1878, p. 218.

Beneke also looks upon the excretion of cholestearin by the liver as a function most important to the œconomy; but he does not, like Dr. Flint, think cholestearin a mere excremental product. Rather noting the wide-spread distribution of this body in both the animal and vegetable kingdom, being found in the seed of both plants and beasts, in the milk, in the chyle, the serum and corpuscles of the blood, in the marrow of bones, and above all in the nervous system, he thinks it must serve other uses than that of a mere excrement. The liver is, according to Beneke, the organ in which cholestearin, and its attendant, lecithin, are formed; with the bile they pass into the intestine, and thence all over the body. In Beneke's view, therefore, cholestearin and lecithin would be two of the most important physiological compounds and certainly the most important of those found in the bile.*

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[*] Tiedemann and Gmelin, *op. cit.* partie i. pp. 395 and 404.

[†] Austin Flint, *Recherches exp. sur une nouvelle fonction du foie*, Paris, 1868. *passim*.

[‡] Hoppe-Seyler, in Virchow and Hirsch's *Jahresbericht f.* 1868, Bd. i. p. 97. See also *Arch. f. path. Anat.* 1863, Bd. xxvi. pp. 527, *et seq.*

To what purpose, then, serves the bile? It cannot be looked upon solely as an excrement, for it has been seen what deep changes in nutrition follow its diversion from the body. There is no evidence that it is necessary for the completion of the process of digestion in the stomach or intestines; indeed it may be said by some physiologists that it does harm to the process in either viscus. The view that it acts as a sort of natural purge has little against it; but, at the same time, there is but little in its favour. As to the power of the bile in arresting putrefaction, it would seem that it must be small, if, as soon as it arrives in the intestine, it begin itself to undergo putrefactive changes. The view that the bile neutralises the acid of the chyme must fall with the establishment of the fact that the bile is not alkaline but neutral in reaction. The only office which remains to it is that of emulsifying fats, a property known to the Greeks 2200 years ago, and of changing starch into sugar. It is melancholy to find that in so many years nothing more is known with certainty as to the uses of this long-studied humour.

It has seemed to me that physiologists are drifting into the belief that the office of the bile is not to act upon the chyme or to assist in the first digestion of aliments. Rather its office is to pass into the intestine, there to undergo changes itself, the products of decomposition being absorbed into the blood, and leaving the body by the urine. If it be admitted that the bile acids be decomposed before they be absorbed, it is most probable that they split up into glycocoll, taurin, and cholalic acid. The glycocoll, it has been seen above, is one of the bodies which, when taken into the intestine, appears in the urine as urea; taurin, in like manner, appears in the urine, probably furnishing the unoxydised sulphur of this secretion, though, according to Salkowski[*] it can no longer be thought that in man it is the source of the oxydised bodies, the sulphates. In rabbits, the ingestion of taurin is still followed by a great excess of sulphates in the urine. The cholalic acid would appear to leave the body by the fæces; but a theory might be made by adopting Schiff's view of a circulation of the bile; supposing a salt of cholalic acid to be absorbed and conveyed to the liver, and there to unite with freshly made taurin and glycocoll, and again to be excreted by the bile. Of the destiny of the bile pigments, little has been yet said; by some it is thought that they undergo oxydation[†] in the intestines; by others, reduction;[‡] but the product of the change, whatever it may be, is called, by Vanlair and Masius, stercobilin;[§] a pigment which is closely allied to that colouring matter of the urine named urobilin by Jaffe.[‖] It thus becomes possible that the bile pigments, after suffering whatever chemical change they may be destined to undergo in the bowel, are absorbed into the blood and excreted by the urine as colouring matter, while the remainder passes out with the fæces. The end of the bile would thus seem to be excretion by the urine; a view not altogether new, for it was taught by physiologists sixteen hundred years ago that the urine was formed in the liver, and separated by the kidneys; and those who come after us may judge whether the nineteenth century have made any real progress in this matter compared with the age of Galen.

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* Beneke, *Grundlinien der Pathologie des Stoffwechsels*, Berlin, 1874, p. 194.

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[*] Salkowski, Virchow and Hirsch's *Jahresbericht f.* 1873, Bd. i. p. 159.

[†] Heynsius and Campbell, *Arch. f. d. ges. Phys.* 1871, Bd. iv. p. 497.

[‡] Maly, *Annalen d. Chemie u. Pharm.* 1872, Bd. clxiii. p. 77.

[§] Vanlair and Masius, *Centralblatt f. d. med. Wiss.* 1871, p. 369.

[‖] Jaffe, *Arch. f. path. Anat.* 1869, Bd. xlvii. p. 423.

CHAPTER VIII.

Action of Drugs upon the Secretion of the Bile.

The notion of a drug which should have a special action on the bile is as old as Hippocrates,* although the word cholagogue does not appear to have been much used before the time of Galen. Certain drugs were commonly supposed in former times to increase the amount of the bile secreted by the liver, because the patient passed stools of yellow or dark colour after the the drug had been administered. It is clear that no reasoning can be more fallacious. The colour of the stools depends not so much on the amount of bile secreted, as on the length of time that the fæces have sojourned in the intestines, or on the diet of the patient. If they should be hurried through the intestines, they may even contain unaltered bile; if the patient have taken abundance of milk, they will be almost colourless. It is plain that no trustworthy information can be had, save from the observation of the amount of bile discharged by a biliary fistula. In man, it has already been said, biliary fistulæ are rare, and in this way knowledge has been but little increased.

In Westphalen's case, indeed, a dose of calomel (1·3 gramme = 20 grains) was once given to the patient, but without causing any increase, rather a decrease, of the amount of bile.† Quinine, given in doses of 2 grammes, (30 grains) could not be found in the bile.

Observations on animals with artificial biliary fistula are, then, the only means by which information is to be had; and Hermann Nasse, the first to make observations on the amount of bile secreted by the dog, was also the first to test the effect of drugs on the bile. He reports that calomel increased the amount of fluid bile but decreased the solids, and that large doses of carbonate of soda decreased both the fluid and solid bile.* As the preparations of mercury are those which have enjoyed the greatest reputation for increasing the secretion of bile, it will be found convenient to discuss them first before the action of other drugs be considered, especially as observers differ, more or less, in their results.

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* Hippocrates, *De nat. hom.* Cap. 5, Littré's ed. t. vi. p. 42.

† Westphalen, *Deutsches Arch. f. klin. Med.* 1873, Bd. xi. pp. 598 and 600.

Nasse, it has been said, appears to have been the first to note the effect of calomel in a dog in whom a biliary fistula had been set up. The observations were made in the month of November, the dog being kept upon the same food throughout, apparently bread and potatoes, and from the 6th to the 15th of the month, carbonate of soda having been added to the food. From Nov. 24 to 27, a gramme of calomel was given within 36 hours with the food. The first day, the dog left half the food set before it; the second, at mid-day, it showed no appetite; but on the third day it left nothing. The amount of bile was less on the first day, but much increased on the two following. The first night, after that the dog had taken ·75 grm. of calomel, the amount of bile secreted, 36·8 grammes, was of a high specific gravity (1015·7).† The mean of the two last days was 212·55 fluid bile, and 4·388 grm. of solid bile. The mean of eight days before the mercury was 126·5 grm. of fluid bile, and 2·887 of solid bile; so that the amount both of fluid and solid bile would seem to be increased.

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* Nasse, *Commentatio de bilis quotidie a cane secreta copia et indole*, Marburg, 1851, p. 18 *et seq.* Those who wish to see the history of opinions on mercury as a cholagogue may consult Dr. Fraser's article in the *Edinburgh Medical Journal*, April, 1871, vol. xvi. p. 904.

† Nasse, *op. cit.* p. 11.

Kölliker and Müller gave four grains of calomel to one of their dogs, at 10 a.m. on the 26th day after the biliary fistula had been set up. Five observations in the afternoon gave as a mean for every half hour 3·823 gr. which was not much over the ordinary average. The next day, four observations gave 3·267 gr. as mean, which was therefore somewhat less than customary. On the 21st and 29th days, the dog was again given four grains of calomel; but the mean of seven observations gave only 2·183 for every half hour. The bile also became brownish and thick so that it would hardly flow. But it should be noted that the dog's health was bad; it was losing weight, and had diarrhœa; the stools were not green but grey; later on they were bloody. For some days the dog would only take bread and milk.*

Dr. George Scott, in 1858, in Dr. Lionel Beale's laboratory, set up a biliary fistula in a dog; he calculated the amount of fluid bile and solid bile secreted in 24 hours, for two days, before calomel was given; and also the average amount secreted in 24 hours, for two days, after the calomel was given. He thought that the action of the calomel would last longer than 24 hours. The bile was collected twice a day, morning and evening. The calomel was given each time after the morning's bile was collected, and therefore the effect of medicine would be upon the bile of the day following. There were four trials of the calomel; and all four gave, in Dr. Scott's opinion, but one result, "a diminution in the amount of fluid bile and bile-solids secreted after the administration of large doses of calomel."†

The details of the experiments made by Dr. Scott are as follows: i. The average amount of bile secreted in 24 hours on June 11th and June 13th, was 1960·7 grains of fluid bile; 104·438 grains of solid bile; and 32·864 grains of bile acids. Three grains of calomel were given at 3 o'clock in the afternoon of June 13th. The average of the two days after giving this dose was 1358·1 grains of fluid bile; 70·4 grains of solid bile, and 26·2 grains of bile acids. Less food was, however, taken after the calomel.

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* Kölliker and Müller, *Verhandlungen der phys.-med. Gesellschaft in Würzburg*, 1855. Bd. v. p. 231.

† George Scott, Beale's *Archives of Medicine*, 1859, vol. i. p. 209.

ii. The bile of 24 hours collected on June 16th was 1639·9 grains in weight: solid bile, 77·599 grains; the bile acids, 12·5 grains. On this day six grains of calomel were given at half past eleven in the morning; the bile collected on June 17th was 518·7 grains in weight; solid bile, 42·18 grains: the bile acids 10·4 grains. No food, however, but 12 ounces of milk was taken on June 17th, and only 9 ounces of water on June 18th, yet the amount of bile collected on June 19th was 817·7 grains of fluid bile; 61·7 grains of solid bile; and 27·486 grains of the bile acids. Thus it would seem that merely withholding food would not cause such a great decrease as was seen after the calomel.

iii. On the 2nd and 3rd of July, the average quantity of bile for 24 hours was 3044·8 grains of fluid bile; 139·2 grains of solid bile, and 61·9 grains of bile acids. The third dose of calomel, 10 grains in amount, was given at half past four on July 3rd. The average for 24 hours of the bile passed on July 4th and 5th was 2720·9 grains of fluid bile; 135·4 grains of solid bile; and 70·6 grains of the bile acids. The bile acids, it should be noted, were thus increased.

iv. On the 6th and 7th of July, the average quantity of bile for 24 hours was 2658·6 grains of fluid bile; 117.7 grains of solid bile; 57·4 grains of bile acids. Twelve grains of calomel were given at six o'clock in the afternoon of July 7th. The average of July 8th and 9th for 24 hours was 1728·9 grains of fluid bile; 85·6 grains of solid bile; and 45·9 grains of the bile acids.

The Edinburgh Committee praise Dr. Scott for the careful and scientific way in which he has made these experiments, and I think every one who is able to judge of these matters will more than agree with them on this point. They, however, look upon Dr. Scott's observations as valuable contributions to the study of the influence of calomel on the bile rather than data which in themselves warrant any conclusion. They think that the diminution of the bile is not nearly so great as Dr. Scott would make out.

The Edinburgh Committee, appointed by the British Association for the Advancement of Science to investigate the action of mercury on the bile, began their work by questioning if mercury have the same action on dogs as on man. The injection of corrosive sublimate under the skin of dogs brought out the same symptoms as in man; salivation, discharge of mucus from the nostrils, fœtid breath, and ulceration of the gums. All these symptoms appeared whether a biliary fistula had or had not been established. In all the dogs without a biliary fistula profuse diarrhœa was caused. In the dogs with biliary fistula, diarrhœa was slight in one and entirely absent in the other two. The Committee conclude that the action of mercury on the dog is the same as that on man.

Their next experiments were on the action of blue pill. In one dog, the mean amount of bile escaping from a biliary fistula in 24 hours from June 11th to June 19th was 119·76 grammes, of which 7·622 grammes were bile solids and 1·259 gramme inorganic salts;* from June 29th to July 4th, the mean was 131·31 grammes, of which 4·71 grammes were bile solids;

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* By inorganic salts is meant the residue left after incineration of the bile.

and 1·343 gramme inorganic salts. From July 9th to July 17th 5 grains of blue pill were given daily, and the mean for 24 hours during this time was 127·6 grammes of fluid bile, of which 5·16 grammes were solids, and 1·38 gramme inorganic salts. Another series of observations was made, but accidents rendered it valueless.

Much the same results were attained with calomel. During 7 days from Sept. 21st to Sept. 27th the mean of fluid bile flowing from a fistula was 82·46 grammes, of which 5·31 grammes were solids, and 1.042 gramme inorganic salts. From Sept. 28th to Oct. 3rd, calomel was given to the dog in doses of two grains, once, twice, or three times a day. The mean of fluid bile during the first four days was 60·02 grammes. The effect of the calomel on the health of the dog was very decided, and it died on Oct. 5th.

It was then determined to note the effect of small doses of calomel frequently repeated. The mean of four days before the calomel was given was 70·62 grammes of fluid bile; of which 3·792 grammes were solids, and 0·83 gramme inorganic salts. On Oct. 30th seven pills were given; each pill held $\frac{1}{12}$ grain of calomel. An hour passed between the giving of each pill. In the same way 14 pills were given on Nov. 1st, and 6 pills on Nov. 2nd. The calomel rapidly acted on the health, and the dog died on Nov. 3, food having been refused for three days before. But no change in the amount of bile was seen: the mean of the four days after the calomel was almost the same as the mean of the four days before: 70·32 grammes of fluid bile, 3·732 of solids, and 0·89 gramme of inorganic salts.

Another experiment was made with calomel in doses large enough to cause purging. The average of six days before the calomel was given was 357·4 grammes of fluid bile, 13·11 grammes of solids, and 3·12 grammes of bile salts. Ten grains of blue pill were then given to the dog, and the three following days ten grains of calomel were given daily. The two first doses of mercury caused slight purging; the two last caused marked purging. During these four days there was an undoubted decrease of the amount of bile. The mean was 272·67 grammes of fluid bile; 7·78 grammes of solids; and 2·06 grammes of inorganic salts. The health of the animal was unaffected by the purging.

Some experiments were also made with corrosive sublimate. The mean, during three days before the corrosive sublimate was given, was 105·4 grammes of fluid bile; 4·144 grammes of solids; and ·948 gramme of inorganic salts. On the 4th day, two doses, of ⅘ grain of corrosive sublimate were injected under the skin of the dog, the first at 1 p.m., the second at 9 a.m. the next day. The bile secreted in the 24 hours under the influence of this corrosive sublimate was 78 grammes; the bile solids were 3·178 grammes and the inorganic salts ·717 gramme. The dog died during the night after the second dose, having shown general tremor, purging with bloody fluid stools, and discharge from the nose.

The next trial was with smaller doses. The mean of three days was 127·15 grammes of fluid bile; 6·43 grammes of solids, and 1·03 gramme of inorganic salts. For ten days corrosive sublimate was injected under the skin; the first three days ⅙ grain in single doses daily; the remaining seven days, twice daily, save that the last dose injected was ⅓ grain. The mean during these ten days was of fluid bile, 113·8 grammes; of solids, 5·972 grammes; and of inorganic salts, ·99 gramme. The health of the animal did not suffer and its weight continued the same. ⅓ grain was given twice on the 11th day and once on the 12th, and observations were suspended as the dog was then suffering much from the effects of the drug. The fluid bile fell to a fourth, and the bile-solids to a third, of what they had been the day before.

Another experiment of the same kind was carried out with results very much the same.

The Committee conclude that blue pill, calomel, and corrosive sublimate, "when given to dogs in either small, gradually augmented, or in large doses, do not increase the biliary secretion; they do not even influence it so long as neither purgation nor impairment of health are (*sic*) produced, but they diminish it as soon as they do either or both."*

Up to this point, the experiments which have been spoken of have been made on the following plan: a biliary fistula has been set up, and after the dog had regained its health, the amount of bile passed in 24 hours has been collected, in various ways, that used by Dr. Scott being the most accurate, and a mean struck, believed to represent that of health: the drug to be tested, in most cases mercury, was then given; and the amount of bile passed, day by day, measured and compared with that given before the drug. The experiments of Röhrig and Dr. Rutherford have all been made somewhat differently.

In Röhrig's plan, the dogs and rabbits were made motionless by woorara, and artificial respiration set up. This last was carried on with the greatest regularity, as it was found that slight changes in the breathing led also to changes in the manner of expulsion of the bile. A glass cannula was then inserted into the common duct, the gall-bladder pressed upon so as to fill the cannula with bile, and the cystic duct clamped to prevent the return of bile into the gall-bladder. In this way all the bile which passed down the hepatic duct escaped at the end of the cannula, and the quickness or slowness ot the secretion was judged of by counting the seconds between the fall of each drop of bile from the end of the cannula.

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* Edinburgh Committee, *Report of the Thirty-eighth Meeting of the British Association for the Advancement of Science; held at Norwich in August*, 1868. London, 1869, p. 222.

Röhrig says, that with large doses of calomel (20 grains for a dog) it is sometimes, but rarely, seen that the bile will again begin to flow after it have completely stopped; and that the drug is able to increase the secretion, after a certain fashion, if it have only fallen off in amount. He speaks of two cases in which the secretion had completely left off; 20 grains of calomel in emulsion were then given; and in two hours the bile had again begun to flow at the rate of one drop for every 120 or 130 strokes of the metronome; at the end of another hour, there was one drop in 85 or 79 strokes; but in half an hour's time the secretion became less, and in 35 minutes had altogether stopped. Calomel may be more trusted if it be desired only to increase a flow of bile which has not entirely ceased; and in this respect the drug gives much the same results as sulphate of magnesia, which, according to Röhrig, acts feebly on the secretion of bile; but his single experiment on this point does not seem to me worthy of very great attention.*

Dr. Rutherford modified Röhrig's process so far that the amount of secretion was not measured by the time that passed between the fall of each drop but by the amount of secretion itself, received in a finely graduated tube. The trials were always made on dogs which had fasted for 18 hours, and which were motionless with woorara.† Several experiments were made with mercurial salts. Ten grains of calomel in 7 C.C.

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* Röhrig, Stricker's *Medizinische Jahrbücher*, Wien, 1873, p. 254.

† Rutherford and Vignal, *Experiments on the Biliary Secretion of the Dog*, p. 1. Report attached to the *British Medical Journal*, 1875, vol. ii.

of water were injected into the duodenum of a dog weighing 19·1 kilogrammes, and an increase of the biliary secretion followed. For two hours before the calomel, the amount of bile secreted was 3·35 C.C., in two hours immediately after, it was 4·25 C.C. After a second dose of ten grains of calomel, the secretion again rose to 4·72 C.C. in two hours. In three other experiments with calomel, no increase was seen; in one, there was a decrease; in the second, no increase; in the third, three grains only were given; and in three-quarters of an hour after the first dose, an increase took place; but the value of this increase is doubtful, as quite as great an increase had taken place before the calomel was given. Two more doses of three grains were given, and were followed by a decrease of the amount of the bile and of the percentage of solids.*

Later on in the series of experiments, the calomel was given mixed with bile. Calomel is said to be slightly soluble in this humour; and it might be asserted that, owing to the absence of bile from the intestines, the calomel could no longer act, as it had no longer a solvent. In two experiments the calomel, even when mixed with bile, and placed in the duodenum, did not increase the amount of bile.

It was suggested to Professor Rutherford that, the calomel being introduced into the duodenum, the action of the gastric juice was avoided; and that the action of the gastric juice might be to convert the calomel into corrosive sublimate. It was found, in fact, that five grains of calomel, if digested for 17 hours in a 2 *per mille* solution of hydrochloric acid, at the temperature of the human stomach, would yield $\frac{1}{35}$ grain of corrosive sublimate. Some experiments were accordingly made with corrosive sublimate. In the first, a dog, weighing 8·8 kilogrammes, had $\frac{1}{20}$ grain, $\frac{1}{15}$, $\frac{1}{15}$, $\frac{1}{20}$, $\frac{1}{15}$,

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* Rutherford and Vignal, *op. cit.* p. 14.

$\frac{1}{16}$ grain of corrosive sublimate, dissolved in 3 C.C. of water, injected into the duodenum at intervals. Altogether $\frac{2}{5}$ grain were given. A slight increase followed the fourth dose; but the result of the whole experiment may be looked upon as negative. But in the next two experiments quite a different result appeared. A little bile was added to the solution of corrosive sublimate. After the injection of this body, in $\frac{1}{16}$ grain doses, into the duodenum of dogs weighing 16 and 17 kilogrammes, the amount of bile secreted rose to a surprising height, from ·17 or ·20 the kilogramme of weight, to ·47 or ·55 the kilogramme. Two more experiments were made with a mixture of corrosive sublimate and calomel in bile. In the first of these there was some increase, and in the second, an immense rise in the quantity of bile secreted. A final experiment with corrosive sublimate alone was made; but the results, from the great variations of the amount, whether corrosive sublimate were given or not, cannot be looked upon as proving much.*

Seeing, then, that corrosive sublimate has a decided action on the secretion of bile, and that some part at all events, of calomel, exposed to the action of hydrochloric acid of the same strength as the gastric juice, is turned into corrosive sublimate, it becomes a matter of speculation whether calomel might not, if introduced into the stomach, act on the liver by a partial conversion into corrosive sublimate. And I fear I must here state my belief that I do not think this question has been completely answered. Dr. Rutherford injected through the gastric wall of a dog five grains of calomel, and says "the result of the experiment was entirely negative, both as regards the liver and intestinal glands," that is, no purgative action was caused by the calomel. It will be admitted on all hands that calomel commonly has a purgative action; but if no purging was caused in this case, why should the effect on the liver, if any, be seen? After the death of of the dog, the calomel was found "apparently unchanged, enveloped in the mucus of the stomach." I am informed that, in the present state of chemistry, the estimation of mercurial salts in organic fluids is attended with extraordinary difficulties, and Dr. Rutherford does not seem to have attempted an estimation of this sort. But until this shall have been done, I think it will hardly be possible to deny positively that the action of calomel is not accompanied by some change in its chemical properties.*

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* Rutherford and Vignal, *op. cit.* p. 79, attached to the *British Med. Journal* for July 7, 1877.

Leaving now the discussion of the action of mercury as a cholagogue, unsatisfactory as this may seem, the influence of other drugs upon the secretion of the bile will be considered. It will be convenient to take these medicines in some order; and the results of Dr. Rutherford's observations will be followed as a guide; not only because he has made trial of a far larger number of drugs than any other observer, but because his results, from the great care and improved methods employed, are more worthy of attention than those of any who have gone before him.

i. The bodies which have no apparent action upon the secretion of bile are the following:

Morphia
Hyoscyamus
Atropia
Tannic Acid
Dilute Alcohol
Bicarbonate of Soda
Iodide of Potassium

Morphia.—Röhrig injected 1·6 C.C. of *tinctura thebaica* into the jugular vein of a dog; the secretion of bile had fallen to one drop in 62 seconds, as the dog had been two hours under observation, and was very weak. Nevertheless, the secretion began at once to rise, and in twenty minutes was one drop in 26 seconds. A like rise was seen after the injection of 4.8 C.C. into the bowel.[*] Dr. Rutherford came to the conclusion that three grains of morphia, injected into the bowel had no influence on the secretion of bile.

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* See a very interesting research by Carl Voit on the manner in which the insoluble calomel is absorbed and acts. (*Phys.-chem. Untersuchungen*, Augsburg, 1857, p. 49.)

Hyoscyamus also has no noteworthy effect on the secretion of bile.

Neither of these bodies interferes with the action of a cholagogue like salicylate of soda; when the salicylate was given after morphia or hyoscyamus, the secretion of bile rose at once to as high a point as if no morphia or hyoscyamus had been given.[†]

Atropia. It is believed by practitioners that belladonna decreases the secretion of the milk and sweat. Dr. Rutherford therefore thought it well worth while to test its action on the bile. It was found, however, to have no immediate action, neither increasing nor decreasing the secretion; and the same result was attained by Laffter, in Heidenhain's laboratory, before the year 1873.[‡] But as atropia antagonises the action of calabar bean in other parts, so it antagonises its action on the liver; calabar bean increasing the amount of bile as well as of the saliva, tears and *succus entericus*.[§]

Carbonate of Soda early attracted notice; from the same reason, apparently, that mercury did: it had been found useful in the bilious state, that is, acute or chronic gastric catarrh, and so, by a natural blunder, connecting bilious disorders with the bile, carbonate of soda was thought to have some special action on the bile.

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[*] Röhrig, *op. cit.* p. 272.

[†] Rutherford, *British Medical Journal*, 1879, vol. i. p. 135.

[‡] Th. Laffter, *Versuche zur Physiologie der Gallensecretion*, Diss. Inaug. Breslau, 1873, p. 22. He came to no trustworthy results with calabar bean.

[§] Rutherford, *British Med. Journal*, 1878, vol. ii. pp. 861 and 909.

Hermann Nasse added on the first day to the food of the dog on whom he had made a biliary fistula 2·5 grammes (37 grains) of carbonate of soda. On the third and fourth days, 1·25 gramme (about 18 grains) was given. On the three following days the food and carbonate of soda were increased by one half. During the first days when the large doses were given, the amount both of fluid and solid bile was much decreased.* Röhrig also finds that carbonate of soda causes a decrease for several hours of the amount of bile secreted both in rabbits and dogs.† Dr. Rutherford, on the other hand, found that bicarbonate of soda feebly increased the amount of bile secreted. In his two experiments the amount of bile slightly rose after each dose.‡

ii. It was formerly thought that the drugs which caused purging would also increase the secretion of bile, probably because it was believed that unchanged bile appeared in the stools. An ingenious anonymous writer§ explains the good effects of purging by the following hypothesis: the bile, if we follow Schiff's observations, is continually making a circulation between the liver and the intestines: first being poured into the duodenum, then absorbed from the intestines into the blood, then carried by the blood to the liver again, and by this organ again excreted into the duodenum: purgatives act by breaking this vicious circle; they hurry the bile through the intestines, not letting it rest long enough in the intestine to be absorbed, and so the patient is relieved from the excess of bile.

It was stated by Röhrig that purging by itself increased the amount of bile ;‖ but the Edinburgh

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* H. Nasse, *op. cit.* p. 9.

† Röhrig, *op. cit.* p. 271.

‡ Rutherford, *British Med. Journal*, 1879, vol. i. p. 105.

§ Probably Dr. Lauder Brunton, *British Med. Journal*, 1873, vol. i. p. 15.

‖ Röhrig, *op. cit.* p. 249.

Committee[*] and Dr Rutherford[§] came to the opposite conclusion; and in this matter, as in many others, I should be inclined to accept their results rather than those of Röhrig. The drugs, which increase the intestinal fluid, but have no action on the bile, are:

Calomel
Gamboge
Sulphate of Magnesia
Sulphate of Manganese
Castor Oil
Chloride of Ammonia
Menispermin

Sulphate of Magnesia. This salt is said by Röhrig to have a slight influence on the bile, raising the secretion from one drop in 98 seconds to one in 34.[‡] Dr. Rutherford, however, finds that sulphate of magnesia has no action as a cholagogue, but that the secretion of bile is diminished when purging comes on.[§]

Castor Oil. Röhrig[||] and Rutherford[¶] agree that Castor oil is almost without influence upon the amount of bile secreted.

iii. The only body the primary action of which is known to cause a decreased secretion of bile is:

Acetate of Lead. Both Röhrig and Dr. Rutherford hold that this has a direct depressing effect upon the secretion of bile. In Röhrig's hands it was noted that when acetate of lead was injected into the intestine of a dog the secretion fell from one drop in 21 seconds to one in 50 or more.[**] Dr. Rutherford injected fifty grains of acetate of lead, in doses of ten grains each, into the duodenum of a dog and found a decided fall after every dose. The fall was not due to the liver being exhausted; for a dose of salicylate of soda caused the amount of bile to rise to a point higher than it was at the beginning of the experiment.[††]

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[*] Edinburgh Committee, *op. cit.* 229.

[†] Rutherford and Vignal, *op. cit.* p. 17.

[‡] Röhrig, *op. cit.* p. 254.

[§] Rutherford and Vignal, *op. cit.* p. 73.

[||] Röhrig, *op. cit.* p. 255.

[¶] Rutherford and Vignal, *op. cit.* p. 16.

[**] Röhrig, *op. cit.* p. 270.

[††] Rutherford, *Brit. Med. Journal*, 1878, vol. ii. p. 945.

iv. The following drugs are able feebly to raise the secretion of bile :

Croton Oil
Senna
Taraxacum
Scammony
Chloride of Sodium
Bicarbonate of Potash
Jaborandi

Croton oil. Röhrig held croton oil to be one of the most active cholagogues ; and it stands at the head of his list. A "teaspoonful," diluted with olive oil and thrown into the duodenum, called forth in an hour and a half an active secretion of bile, so that one drop fell from the cannula every three seconds. In other experiments the bile was very viscid and the drops could not be counted.* With smaller doses, Dr. Rutherford found different appearances. After fifteen grains of croton oil (about 30 drops,) diluted with sixty minims of almond oil, were injected, a fall took place ; with six grains, no decrease or increase ; with three grains, a decided increase.†

Senna was found by Röhrig to have an active effect on the secretion of bile. After a dose of 15 grammes in 150 C.C. of fluid, the bile, from dropping once in every 60 seconds began in an hour to drop once in 4 to 5, although this great rapidity lasted but a short time and was followed later on by complete stopping of the secretion.‡ Dr. Rutherford, however, found very little change in the secretion before and after the giving of senna in three experiments ; and if any, the bile contained less solids.§

Taraxacum. This drug was found by the Edinburgh Committee to be tolerably inert. They report that doses of the solid extract varying from 60 to 240 grains had no influence upon the bile nor the health of the dogs ; nor did they cause purging.‖ Dr. Rutherford's further experiments agree with this statement.¶

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* Rohrig, *op. cit.* p. 250.

† Rutherford and Vignal, *op. cit.* p. 3.

‡ Röhrig, *op. cit.* p. 254.

§ Rutherford and Vignal, *op. cit.* p. 10.

‖ Edinburgh Committee, *op. cit.* p. 229.

¶ Rutherford and Vignal, *op. cit.* p. 13.

Chloride of Sodium. Dr. Rutherford made only one experiment with this drug, four doses of 120 grains each being injected into the duodenum. The amount of bile was very feebly increased.[*]

v. The following are the bodies which markedly increase the secretion of bile:

Aloes
Podophyllin
Rhubarb
Colchicum
Colocynth
Jalap
Ipecacuanha
Benzoates
Salicylates
Sulphates of Soda and Potash
Phosphates of Soda and Ammonia
Dilute Nitrohydrochloric Acid
Corrosive Sublimate
Muscarin
Nicotin
Calabar Bean
Euonymin
Sanguinarin
Iridin
Leptandria
Baptisin
Phytolaccin
Hydrastin
Juglandin

Aloes. After mercury, the preparations of aloes have received most attention from different observers. Kölliker and Müller gave one of their dogs one grain of extract of aloes on one day, and two grains on the following, but they hardly noted any change in the amount of bile daily secreted.[†] Röhrig tested, with his method, the action of aloes on a dog and a rabbit. No details are given of the experiment on the dog, in which the action of aloes is said to resemble that of jalap. In a rabbit, 3 grammes of aloes dissolved in 7·5 grammes of water were injected into the small intestine. In 70 minutes, the secretion of bile, which had ceased before the solution of aloes was given, began again, 79 to 77 seconds passing between the fall of each drop; an hour after this, 26 to 13 seconds only between each drop; in a short time the secretion began to fall off, and in an hour had completely stopped.[‡]

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[*] Rutherford, *Brit. Med. Journal*, 1879, vol. i. p. 71.

[†] Kölliker and Müller, *op. cit.* p. 231.

[‡] Röhrig, *op. cit.* p. 252.

Dr. Rutherford also found a great increase of bile, marked in 30 minutes after aloes had been given. Though the bile was rendered more watery, yet a greater amount of solids was excreted. The experiments were made on two dogs into whose duodenum sixty grains of aqueous extract of Socotrine aloes in watery solution were injected.[*]

Podophyllin. The action of this drug upon dogs with biliary fistulæ was first investigated by the Edinburgh Committee. They report that doses of podophyllin, varying from 2 to 8 grains, given to dogs, caused a decrease of the solid bile, whether purging came on or not. Doses which caused purging also caused a decrease in the solid and fluid parts of the bile.[†] This is the only part of the report on podophyllin which coincides with the experiments made by Dr. Rutherford later on. On the contrary, he found that podophyllin injected into the duodenum increased the flow of bile in seven experiments, and that this flow of bile is greater when bile also is present in the duodenum. The mucous membrane of the intestine was usually much reddened.[‡]

Rhubarb was found by Röhrig to raise the secretion of bile from one drop in every 92 seconds to as much as one drop in every 9 seconds.[§] Dr. Rutherford also found rhubarb a remarkable stimulant to the secretion of bile. The injection of rhubarb into the duodenum was always followed by a remarkable rise in the amount of bile, the composition of which remained unchanged.[¶]

Colocynth. Röhrig placed colocynth near the head of his list ot cholagogues; under its influence he saw that a drop of bile fell from the cannula every two or three seconds.[*] Dr. Rutherford finds that colocynth has considerable influence in increasing the secretion of the bile, although it does not seem to be worthy of the very high place given to it by Röhrig. Colocynth increases both the fluid and solid parts of the bile.[*]

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[*] Rutherford and Vignal, *op. cit.* p. 7. [†] Edinburgh Committee, *op. cit.* p. 229.
[‡] Rutherford and Vignal, *op. cit.* p. 8. [§] Röhrig, *op. cit.* p. 253.
[||] Rutherford and Vignal, *op. cit.* p. 4. [¶] Röhrig, *op. cit.* p. 252.

Jalap. Next to colocynth as a cholagogue Röhrig set jalap[†] and Rutherford agrees with him that the drug is a considerable stimulant to the secretion of bile, though its chief action is on the intestinal glands.[‡]

Benzoates and Salicylates. The study of the physiological action of these bodies upon the liver is interesting. In their chemical composition they are allied. They both combine with glycocoll, the base of one of the bile acids, to form hippuric and salicyluric acid.

Benzoic acid has been long employed in the treatment of jaundice, and it was made the subject of some experiments by Kühne about twenty years ago. He thought that in jaundice benzoic acid passed out by the urine unaltered instead of combining with glycocoll to pass out as hippuric acid.[§] Kühne's theory was, however, soon disproved, as the presence of the benzoic acid in the urine was found to be due to the decomposition by putrefaction of the hippuric acid. It is, therefore, noteworthy that both benzoates and salicylates greatly increase the secretion of bile by the liver, and are among the most active of the drugs investigated by Dr. Rutherford; and his results on this point are perhaps the most interesting to the physiologist of all that he has published. Benzoic acid, itself, apparently owing to its insolubility, has but slight action on the bile, while the soda and ammonia salts at once raise the amount secreted.[||]

Muscarin. Prevost says that a few milligrammes of muscarin injected into a vein cause a notable increase of the bile in a dog. Atropia, however, antagonises this effect.*

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[*] Rutherford and Vignal, *op. cit.* p. 69.

[†] Röhrig, *op. cit.* p. 252.

[‡] Rutherford and Vignal, *op. cit.* p. 72.

[§] Kühne, *Arch. f. path. Anat.* 1858, Bd. xiv. p. 318.

[||] Rutherford, *British Medical Journal*, 1879, vol. i. p. 69.

Nicotin. Laffter found, in Heidenhain's laboratory, that 3 drops of nicotin in 50 grammes of water, injected into the jugular vein of a dog, cause an immediate but short increase of the bile. This appearance was thought due to the contraction of the ducts, and consequent expulsion of bile.†

Euonymin, Iridin, etc. The eight drugs mentioned last on the list come from American sources, and iridin and euonymin are specially active in increasing the secretion of bile, as will be seen by the following table. This table has been borrowed from Dr. Rutherford, and he remarks, that a drug may be looked upon as a powerful cholagogue if it raise the hourly secretion of bile for every kilogramme of body weight to 0·4 C.C.

Drug.	Total dose in grains.	Dose in grains for kilogramme of body weight.	Secretion of bile for kilogramme of body-weight: an hour.	
			Before. C.C.	After, C.C.
Normal secretion of bile during the influence of small doses of woorara			0·35 0·25 0·15	
Podophyllin	6 without bile	0·9	0·04	0·47
,,	4 with ,,	0·23	0·52	1.01
Aloes	60 without ,,	6·9	0·34	0·69
,,	60 ,, ,,	12·0	0·26	·93
Rhubarb	68 ,, ,,	3·06	0·17	0·32
Colchicum	60 ,, ,,	2·5	0·13	0·45
Euonymin	5 with ,,	0·26	0·25	0·47
,,	5 ,, ,,	0·21	0·07	0·46
Sanguinarin	3 ,, ,,	0·11	0·16	0·30
,,	1 ,, ,,	0.05	0·12	0·40
Iridin	5 ,, ,,	0·22	0.22	0·53
,,	5 ,, ,,	0·92	0·16	0·63
Leptandria	18 ,, ,,	1·4	0·08	0·31
Ipecacuanha	60 ,, ,,	2·2	0·24	0·55
,,	3 ,, ,,	0·49	0·18	0·38
Colocynth	14 ,, ,,	0·53	0·20	0·45
,,	7 ,, ,,	0·4	0·16	0·27
Jalap	30 ,, ,,	1·2	0·16	0·29
Sodium sulphate	508 ,, ,,	32·3	0·25	0·38

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* Prevost, *Comptes rendus*, 1874, t. lxxix. p. 381.

† Laffter, *Versuche zur Physiologie der Gallensecretion*, Diss. Inaug. Breslau, 1873, p. 24.

Drug.	Total dose in grains.	Dose in grains for kilogramme of body weight.	Secretion of bile for kilogramme of body-weight: an hour.	
			Before C.C.	After C.C.
Potassium sulphate	232 without bile	10·7	0·31	0·47
Sodium phosphate	201 ,, ,,	7·4	0·27	0·44
Rochelle salt	463 with ,,	37·0	0·23	0·33
Dilute nitro-hydrochloric acid	36·4 without ,,	2·0	0·11	0·39
Mercuric chloride	⅛ with ,,	0·0077	0·17	0·47
,, ,,	,, ,, ,,	0·0071	0·20	0·55
{ Mercuric chloride	$\frac{1}{20}$,, ,,	0·005 }	0·48	0·72
{ Calomel	1 ,, ,,	0·101 }		
{ Mercuric chloride	$\frac{1}{30}$,, ,,	0·0027 }	0·22	0·85
{ Calomel	1 ,, ,,	0·054 }		
Extract of physostigma	2 ,, ,,	0·0074	0·09	0·36
,, ,,	2 ,, ,,	0·0147	0·13	0·75
Baptisin	7 ,, ,,	0·303	0·23	0·39
,,	7 ,, ,,	0·374	0·12	0·29
Phytolaccin	2 ,, ,,	0·064	0·144	0·29
,,	2 ,, ,,	0·104	0·338	0·47
Hydrastin	2 ,, ,,	0·077	0·23	0·38
,,	2 ,, ,,	0·147	0·09	0·32
Juglandin	5 ,, ,,	0·236	0·10	0·28
	10 ,, ,,	0·472	0·10	0·32
Sodium benzoate	20 without ,,	1·320	0·22	0·64
Ammonium benzoate	20 ,, ,,	0·737	0·24	0·54
Sodium salicylate	20 ,, ,,	1·000	0·17	0·56
,, ,,	25 ,, ,,	1·550	0·26	0·66
,, ,,	20 ,, ,,	2·150	0·32	0·89

Dr. Rutherford does not profess to be able to explain the exact manner in which the cholagogues that he names act. The gall-bladder and the gall-ducts may be the means by which a more rapid expulsion of the bile may be brought about; and if these be excited by drugs, that might be one way in which cholagogues act. But it will be said that in Dr. Rutherford's experiments, the gall-bladder and gall-ducts were thrown out of play. It may be acknowledged that the gall-bladder was excluded; but I should feel hesitation in accepting the same statement as to the hepatic ducts; indeed the diagrams of the action of some of the drugs look like the result of a sudden contraction of the ducts. But excluding the action of the ducts, there would remain three hypotheses: (i.) that the cholagogues, the action of which Dr. Rutherford has investigated, excite the mucous membrane of the duodenum and thereby cause a greater secretion of bile from reflex excitement of the liver. Something like this is seen in the action of sialagogues, which cause a great flow of saliva by acting on the buccal mucous membrane. Against this theory is the fact that those drugs which most actively excite the intestinal mucous membrane do not excite the secretion of the liver; while the most active cholagogues are those which have no influence on the mucous membrane: (ii.) that these cholagogues increase the flow of blood through the liver; a theory thought to be opposed to the fact that an increased flow of blood to the intestines is not followed by increased secretion of bile. But an excess of blood in the intestines is followed, not always by an excess of blood, but sometimes by a want of blood, in the liver: or (iii.) that these cholagogues have a direct action upon the cells or nerves of the liver, a theory to which Dr. Rutherford is himself inclined.

It has been seen that the wish to increase the amount of bile excreted by the liver comes of a most venerable antiquity; but it may now be asked: in what diseases or in what states would good be done to a patient if the amount of bile poured into the duodenum were increased? It seems to me that it would be judicious to put aside at once all organic diseases of the liver, such as cirrhosis, amyloid degeneration, and the like; for in them the same kind of evil would follow the use of a stimulant to the liver, as of certain diuretics in Bright's disease; and one of the first rules of medicine, to give diseased parts rest, would be broken. Then in cases of jaundice, it would surely be undesirable to attempt to increase the secretion of bile; for the bile passages being already over-filled, harm would be done by pouring fresh bile into them. Then comes the long list of disorders which the public love to think due to "the bile," and call "biliousness," the symptoms of which are really due to a catarrhal state of the gastro-duodenal mucous membrane, as will be seen in the chapter on bilious disorders. Would an increased secretion of bile be good in a bilious disorder, that is, gastro-duodenal catarrh? I cannot appeal to experience on this matter; but if it be safe to hazard a conjecture beforehand, it would seem improbable that the pouring of a fluid like bile over an inflamed mucous membrane would relieve it; and an effectual remedy is already known in a single mercurial purge, followed by a gentle alkaline course. Dr. Rutherford says he has found very decided benefit from administering four grains of iridin at bedtime in cases of "biliousness;" the patients awaking in the morning and finding the headache and malaise gone, and the yellow tongue clean; and he also recommends that a dose of Püllna water be taken after the iridin, and that iridin be not taken oftener than once a week, as it leaves a somewhat depressant effect behind it. Instead of iridin, Dr. Rutherford would seem rather inclined to favour euonymin in two-grain doses, and says that he has "been much struck with the success of euonymin in functional hepatic derangement, in several persons who had tried nearly all the commonly used cholagogues with varying and often very limited success."[*]

There is one state in which I can well imagine that an increase of bile might be useful; and that is at the end of an attack of jaundice when the stools have begun to shew some appearances of returning colour, but the conjunctiva, skin, and urine of the patient still remain yellow. In this case a stimulus to the secretion of bile may possibly be of much use; and in former times the benzoates have been successfully used for this purpose.

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[*] Rutherford, *British Medical Journal*, 1879, vol. i. p. 178.

I know that functional hepatic derangement is often talked about; and I fear that some will think it a disgraceful confession when I own my entire and complete ignorance of this pathological state. I have never met with it in the *post-mortem* room and I do not know how it can be recognised during life. Precise and accurate information as to the clinical state, called by some practitioners congestion of the liver, torpor of the liver, or sluggish action of the liver, is also wanting; and also the appearances seen after death in these diseases; or if they do not prove fatal, the grounds on which the symptoms are linked to a disturbance in the functions of the liver.

If the office of the bile were better known, it would be easier to say in what states an increase of this humour may be wished for. Modern physiology seems rather to be on the way of returning to the opinion of Aristotle that the bile is an excrement, though not an immediate excrement, as great part of it is again absorbed into the blood. The bile is now thought to have little influence on the digestion of the food. But it may hereafter be proved to play an important part in the metamorphosis of the tissues; and then the amount of bile secreted will enter into the calculations of the scientific physician. Until Dr. Rutherford began his series of researches, the prescriber of drugs was altogether without trustworthy knowledge, whenever he wished to increase the amount of bile secreted. There was nothing to guide him but the tradition of the power of calomel. Now there is a certain foundation to build on, and Dr. Rutherford's results and method are the beginning of a new and reasonable system of hepatic therapeutics.

Though somewhat foreign to the subject of this chapter, yet it may be convenient here to consider whether any drugs have the property of causing unchanged bile to appear in the stools. It will, I suppose, be granted by the chemists that in health the unaltered bile pigments cannot be found in the fæces. Yet there can be no doubt that the colour of the fæces in health is due to the presence of the bile, however much the pigments may be changed; for if the bile duct of an animal be tied, or if in man disease obstruct the duct, the fæces at once lose their natural colour and become white. But between acknowledging that the colour of the fæces in health is due to the bile, and that all the variations in colour seen in disease are due to the bile, there is a wide distance. Formerly a high colour was thought evidence of increase of bile in the fæces. Purgatives often bring away high-coloured stools; therefore purgatives increase the amount of bile in the fæces.

This reasoning should, however, long have been abandoned. It is well known that many drugs given by the mouth cause the fæces to become black; for example, charcoal, iron, bismuth; and that the presence of blood gave a black colour to the stools was known to Hippocrates.

The want of colour in the fæces is almost universally set down to a decrease in the secretion of bile. But I should like to point out that of this there is no evidence. The absence of bile is, no doubt, the cause of the white stools in jaundice; but it would be highly imprudent to assert that it is the only cause of want of colour in every disease. In many kinds of brutes, the fæces are grey or even white in health, and in some of these, as in the dog, there is evidence that the liver is as active as in man. The colour of the fæces, then, is not due to the want of the secretion of bile; it is rather more likely to be due to the absorption of the bile after it have passed into the intestine. Then on certain diet, as milk, the stools often become light coloured; yet there is no evidence of a decreased secretion of bile, or of an increased absorption of bile from the intestine. It is easy to imagine a cause for this lack of colour, but there is no certain knowledge about it.

In judging of the presence or absence of bile in the fæces, chemical analysis is, in my opinion, the only trustworthy guide.

It is well known that calomel, in purgative doses, brings away stools of a peculiar green colour, compared to that of spinach. Michéa attempted by a chemical analysis to prove that this colour is due to the presence of bile. He discarded Pettenkofer's test, as he found it troublesome to apply; but availed himself of the well-known reaction of the bile pigments with nitric acid. He found no play of colours in the stools of healthy men and women; but in one case of *embarras gastrique* out of three, the action was distinct enough in the vomited matters and green stools. Calomel was given to eight persons suffering from constipation: in four, green stools were passed; and in two of these four, nitric acid detected the presence of bile. Sulphate and phosphate of soda, jalap, and castor oil were given, but the stools had not the green colour of calomel stools, nor did nitric acid give the peculiar reaction.* Radziejewski, on the other hand, gave calomel to a dog with a biliary fistula, in which, therefore, no bile could enter the intestine; and saw the accustomed loose stools of a green colour, but in these no bile pigment could be found. It was further shown by Radziejewski that undecomposed bile is but rarely found in the fæces after the action of purgatives of any sort; out of nearly forty experiments on dogs, undecomposed bile was only found four times, after calomel, castor oil, senna, and croton oil, and even then the reaction was somewhat doubtful.† The appearance of the fæces was found in no way to correspond with the results of the chemical analysis. They were often green, and yet gave no reaction with Gmelin's test.

The cause of the green colour of the stools is not well made out. It may very possibly be due to some compound of mercury; for the statement that mercury is not to be found in the fæces cannot be maintained after the observations of Saikowski,* and of Mayençon and Bergeret,† who found that the fæces as well as the urine were the chief vehicles by which mercury leaves the body. A green colour is also seen after some other purgatives besides mercury; for example, in the stools of those who make use of the Carlsbad and Marienbad waters.

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* Michéa, *Union méd.* 1848, t. ii. p. 495.

† Radziejewski, *Arch. f. Anat. Phys. u.s.w.* 1870, p. 37.

Drugs which pass into the bile. Several isolated observations were made before 1858, on the drugs which are found in the bile after being introduced into the œconomy; but it was Mosler who first carried out a definite research on this point. Biliary fistulæ were made in dogs; and in a week or more, the bodies to be tested were either injected into the veins or else given by the mouth.

Albumen was the first body to which attention was directed. Mosler found that it was not a natural constituent of the bile of dogs. On injecting 135 C.C. of warm water into the crural vein of a dog, albumen appeared in the bile in from 2 to 4 hours after the injection; the albumen decreased in amount in 6 to 7 hours after; in 8 hours, only a trace was found; and in 8 to 10 hours, none. The urine showed albumen even half an hour after the injection.

Mosler says nothing of the way in which the albumen was looked for. It is known that the bile acid salts have the property of coagulating albumen.

Mosler satisfied himself that no grape sugar was present in the bile of dogs in health, and that a great quantity must be present in the blood before it appeared in the bile. After 20, 30, and 40 grammes (300 to 600 grains) had been injected into the crural vein, none could be found in the bile while there was abundance in the urine. When 65 to 80 grammes (1000 to 1200 grains) were injected, the dog usually died or was killed; and after death sugar was found in the contents of the gall-bladder.

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* Saikowski, *Arch. f. path. Anat.* 1866, Bd. xxxvii. p. 346.

† Mayençon and Bergeret, *Journal de l'Anatomie et de la Physiologie*, 1873, p. 81.

Cane sugar appears in the bile, as in the urine, more readily. Only 40 grammes need to be injected into the veins.

One gramme (15 grains) of iodide of potassium given by the mouth could not be detected with certainty the same day in the bile. The next day two grammes (30 grains) of iodide were given, and a distinct reaction was found with starch on the third day. In another experiment, one gramme of iodide was given at 7 in the morning; and at 3 in the afternoon, the bile gave distinct signs of the presence of iodine; the bile collected from 3 o'clock to 7 next morning gave no reaction.

Six grammes (about 90 grains) of nitre, given by the mouth, did not cause the bile to show a reaction indicative of the presence of nitrates.

For three days a dog was given twelve grains of sulphate of copper every day, in pills of two grains each every two hours. A trace of copper was found in the bile on the first two days; on the third, however, there could be no doubt about its presence, both in the bile and urine. Mosler thinks that more copper is excreted by the bile than by the urine. Copper, however, would appear to be a constant constituent of bile.

5 and 10 grains of calomel were given by the mouth to a dog; but no mercury was found in the bile collected within 24 hours. A chemist might, however, have something to say as to the method employed for getting rid of the organic matter of the bile; it is quite possible that in getting rid of the organic matter, the mercury also disappeared.

Autenrieth and Zeller found mercury in the bile of a dog, in no very great amount, however, who had been killed by rubbing the metal into the skin. The bile was also singularly thick.[*] C. E. E. Hoffmann, in his inaugural dissertation at Würzburg in 1854, states that he found no mercury with the microscope in the bile or any other part of the animal, after metallic mercury or blue ointment had been given by the mouth or rubbed in. Hoffmann's experiments were made on several animals, dogs, rabbits, and cats, and on one man.[†]

Oesterlen rubbed blue ointment into the skin of a cat and also gave the animal the ointment to eat. He found mercury, apparently in the metallic state, in the liver, and in still greater quantity in the fluid green bile.[‡]

Mayençon and Bergeret used a very delicate test for mercury in their experiments, and they found it in great abundance in the livers of rabbits whom they had poisoned.[§] It seems probable that it would also be found in the bile, if looked for with equal care; and the bile may be one of the sources of the mercury found in the stools.

Quinine was given to a dog in two following days in doses of two grains each, so that in two days the dog had about 16 grains given it, that is, more than one gramme. None of this body could be found in urine or bile of the following day. It must be remembered however that it is very hard to recognise the presence of alkaloids in organic fluids.

For two days 10 grains (·66) grm. of benzoic acid were given to a dog every two hours. Altogether two drachms were given (about 4 grammes.) Hippuric acid was found in the urine but not in the bile.

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[*] Autenrieth and Zeller, Reil's *Archiv f. d. Phys.* 1807 and 1808, Bd. viii. p. 255. This increased thickness was also noted by Roche. (*Dict. de med. et de chir. prat.* Paris, 1830, t. iv. p. 114, art. Bile.)

[†] C. E. E. Hoffmann, *Ueber die Aufnahme von Quecksilber und der Fette in den Kreislauf.* Diss. Inaug. Würzburg 1854. Abstract in Canstatt's *Jahresbericht f.* 1855, Bd. i. p. 80.

[‡] Oesterlen, *Arch. f. phys. Heilkunde*, 1843, Bd. ii. p. 536.

[§] Mayençon and Bergeret, *Journal de l'Anat. et de la Phys.* 1873, année ix. p. 81. Mercury was found in the greatest abundance in the liver and kidneys.

Turpentine was also given to the dog: but although the urine showed the characteristic smell of violets, yet the presence of turpentine could not be determined in the bile. The bile had indeed a peculiar resinous smell, but no chemical proofs could be had.* This observation is important in its bearing upon the use of Durande's remedy, who proposed to dissolve biliary calculi by giving through the mouth a mixture of æther and oil of turpentine.

Iron, it is known, is a constant constituent of the bile. In a man who had made a pratice of swallowing clasp knives, and thus probably introduced metallic iron into his stomach, Marcet found the iron in the bile increased in amount. In 150 grains of this bile, 0·5 grain of prussian blue was found, while in 150 grains of ordinary bile, only 0·2 grain was found.†

Lead was first found by Heller in the bile of a man who had died of chronic poisoning by lead.‡

Annuschat has made some careful experiments to see if this metal can again be recognised in the bile after being given by the mouth. A biliary fistula was established in fourteen rabbits, and lead was given at various times before the establishment of the fistula. Lead was found in the bile, though in small quantity, in all cases in which the metal had been given shortly before the fistula was set up. When the lead had ceased to be given three or more days before the fistula was established, no lead could be found in the bile, though small quantities could be found in the liver.§

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* Friedrich Mosler, *Arch. f. path. Anat*, 1858, Bd. xiii. p. 29.

† Marcet, *Med. Chir. Trans.* 1823, vol. xii. p. 63.

‡ Heller, *Arch. f. phys. u. path. Chemie*, 1845, p. 322.

§ Alb. Annuschat, *Arch. f. exp. Path.* 1877, Bd. vii. p. 45.

CHAPTER IX.

THE PHYSIOLOGICAL ACTION OF THE BILE.

The bile of animals has been used in medicine from the earliest times. In Hippocrates it enters into the composition of pills and other remedies to be taken by the mouth, as well as of pessaries, suppositories, and applications to wounds. In the book of Tobit, it is used as a lotion for opacities of the cornea,[*] and Pliny mentions with horror and reprobation that Miletus had proposed human bile for the same purpose.[†] In these days ox bile has been given in capsules in cases of jaundice; and Röhrig has suggested that in high fever bile acids might be given to bring down the præternatural heat of the body.[‡]

The physiological action of the bile can hardly be said to have been studied until less than 30 years ago. There are indeed some old experiments by Deidier who injected the bile of patients who had died of the great plague at Marseilles into the veins of dogs, and found that the dogs were speedily killed; when swallowed, the bile did no harm;[§] and Magendie shortly states that a gramme of bile rapidly injected into the crural vein will kill an animal in a few moments; but the same quantity injected slowly, or into the *vena porta*, is harmless.[*]

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[*] It is clear that the book of Tobit was written after the Babylonish Captivity; but the latest date given to it by any critic is, I am told, the second century before Christ.

[†] Plinii *Hist. Nat.* Lib. xxviii. cap. ii. "Miletus oculorum suffusiones felle hominis sanari."

[‡] Röhrig, *Arch. d. Heilkunde*, 1863, p. 418.

[§] Deidier, *De bile peste emort. exp.* quoted by Bianchi, *Hist. Hepatica*, Genevæ, 1725, Pars iii. p. 804. According to Haller (*Biblioth. Anat.* t. i. p. 808.) these experiments have been published several times; in *Journal Savans*, 1722, and *Phil. Trans.* n. 370, as well as separately at Zürich and Montpellier.

Bouisson injected some 120 grammes of bile into the stomach of a dog, and then tied the gullet. After ineffectual efforts at vomiting, a diarrhœa was soon set up. Bouisson thinks this experiment aids the theory that the bile is a natural purgative.[†] Everyone, however, who has given drugs to dogs, will have noticed that vomiting and purging follow the administration of almost every kind of drug, whatever be its physiological action: so that little weight can be given to this single experiment.

Goupil injected 16 grammes of bile into the saphena of a dog. Shortly after, a general disturbance and languor showed itself, but became less and less intense, and the animal recovered its health without delay. The injection of the same quantity of bile into the portal vein was followed by no symptoms whatever.[‡] Bouisson, on the other hand, injected six grammes of human bile, taken from the gall bladder, into the jugular veins of rabbits; in three cases, a sort of tetanic stiffness shortly showed itself, quickly followed by death. On dissection, a distension of the right heart, and thrombosis of the pulmonary artery were found. If, however, the bile were filtered before injection, there was a certain amount of stupor and malaise which completely disappeared within half an hour. Bouisson thought that the action of the bile in the fatal cases was merely mechanical, owing to the suspension of particles in the bile too large to pass the capillaries of the lungs.[§] Theodor von Dusch repeated these experiments with filtered bile and found that two rabbits were rapidly killed with tetanus and opisthotonos whether the bile were injected into the crural or the jugular vein; while the injection of filtered bile into the *vena saphena* of a dog was followed only by a few irregular contractions of the muscles, and by vomiting; and in two days the dog had recovered his health.*

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[*] Magendie, *Précis élémentaire de Physiologie*, Paris, 1836, 4e éd. t. ii. p. 259.

[†] Bouisson, *De la bile*, Montpellier, 1843, p. 56.

[‡] Goupil, *Essai sur la physiol. du foie*, Thèse de M. Renaud, Strasbourg, 1838, quoted by Bouisson, *op. cit.* p. 59.

[§] Bouisson, *op. cit.* p. 60.

There can be little doubt that some of these cases of severe symptoms following the injection of unfiltered bile are due solely to the mechanical impaction of solid particles in the pulmonary artery. If, however, the bile have been filtered, the cause of death is probably the same, thrombosis of the pulmonary artery; but the thrombosis is due to the solution of the corpuscles by the bile acids and consequent formation of a clot.†

Johannes Ranke and Sydney found no symptoms follow the injection into the jugular vein of a rabbit of the bile secreted by its own liver.‡ The absence of all appearances is probably due to the small amount of solids in the bile freshly secreted by the liver of vegetable eaters; and not that the bile secreted by the animal itself has no influence over its own œconomy, as these writers believe.

It will be convenient in further dealing with the physiological action of the bile to consider the experiments in sections corresponding with the chemical constitution of this humour; the bile acids, bile pigments, and cholestearin. The bile acids show the most active physiological properties, and may therefore be considered first of all.

PHYSIOLOGICAL ACTION OF THE BILE ACIDS.

It has been explained, in speaking of the chemistry of the bile, that Platner's crystallized bile is a mixture of the soda salts of two acids, taurocholic and glycocholic acid. These two acids differ but little in their physiological action, taurocholic acid being somewhat more active than glycocholic. Feltz and Ritter found that ·46 grm. of taurocholate of soda for each kilogramme of animal would cause death, apparently when injected into the blood vessels; of the glycocholate, ·64 grm. was needed for each kilogramme; while of the mixture of the two salts (Platner's crystallized bile) ·51 grm.[*] Leyden found that less than a gramme of bile acid salts injected suddenly into the heart would at once cause death in a dog. An injection of 3 or 4 grains into the carotid killed a dog in a few minutes. With injections into the blood done slowly, larger doses, nearly 2 grammes, were needed to kill dogs even in one or two days.[†]

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* Th. von Dusch, *Untersuchungen und Experimente als Beitrag zur Pathogenese des Icterus*, u.s.w. Leipzig, 1854, p. 17.

† See below, Action of the Bile Acids on the Nervous System.

‡ Johannes Ranke, *Die Blutvertheilung und der Thätigkeitswechsel der Organe*, Leipzig, 1871, p. 173.

Johannes Ranke has stated that 15 milligrammes are enough to kill rabbits when injected into the jugular vein. In this mode of death, the bile acid salts kill, not by a specific action on the heart, but by causing a thrombosis of the pulmonary artery.[‡] I cannot, from my own observations, confirm Johannes Ranke's statement, as I have found rabbits bear much larger doses with impunity.

In these acids, the active body would seem to be the cholalic acid; it acts upon the heart and dissolves the red corpuscles with energy, while glycocoll and taurin have been found to be almost inert.

Organisms, apparently fungi, were seen in solutions of the bile acids in water after the solution had been kept for some weeks. But their growth is not rapid.*

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[*] Feltz and Ritter, *Journal de l'Anatomie et de la Physiologie*, 1874, t. x. p. 583. These writers do not expressly say whether the doses were injected under the skin or into the blood; apparently into the blood. Still less do they say into what vessel, whether the jugular or crural vein; and yet this is a matter of some importance.

[†] Leyden, *Beiträge zur Pathologie des Icterus*, Berlin, 1866, p. 99.

[‡] Johannes Ranke, *Die Blutvertheilung und Thätigkeitswechsel der Organe*, Leipzig, 1871, p. 164.

General Experiments: on the frog. If one cubic centimetre of a 10 or 12 *per cent.* solution of Platner's crystallised bile be injected under the skin of a frog, he at once begins to jump about as if much excited. In about five minutes, however, the movements become less active and in ten to twenty minutes the frog is motionless, unless he be touched or made to move. The next appearance is that the hind limbs begin to abide where set by the observer; and with great trouble he draws the legs up when they are extended by observer. He no longer springs but crawls: and if put on his back cannot recover himself. He shows no movements but those of respiration. In a couple of hours or so he is commonly found lying relaxed, no longer in the sitting posture, with pupils contracted, and showing very little or no reflex action.†

These phænomena may appear sooner or later. The frog may die in a few hours; or last on until the third day.

In the advanced stage of the action of the bile acids upon frogs, I have found that electrical irritation of the nerves or muscles was commonly followed by lively contractions; in some instances, however, I have seen no movement follow.

I have also repeated with the same results an experiment first made by Leyden. A frog was put into a vessel holding enough of a 1. *per cent.* solution of bile acids to cover the bottom. The frog was always found dead the next morning, and on examination with the microscope parenchymatous changes were found in the heart and liver.

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* See p. 145 on the arrest of putrefaction by the bile acids.

† In these I give a summary of my own experiments. It would be tedious to give the details of each. See also Leyden. (*Beiträge zur Pathologie des Icterus*, Berlin, 1866, p. 57.)

Injections under the skin of the rabbit. Leyden found that rabbits died without fail in 2 or 3 days after the injection of 6 C.C. of a 10 *per cent.* solution under the skin. Immediately after the injection there was excitement, just as with frogs, which also soon disappeared. On the first day, the rabbits took their food; on the second, not; and they became listless. Death sometimes took place in the midst of convulsions. Bile acids were found in the urine by using Hoppe's method, but not bile pigment.[*]

Injection into the Stomach. Both Röhrig[†] and Leyden[‡] have injected as much as one or two grammes of the soda salts of the bile acids into the stomach of rabbits. Röhrig noted no symptoms, while Leyden observed a diarrhœa to be set up, which apparently killed the animal on the 7th day after the injection. No bile acids or bile pigments were found in the urine. No morbid appearances were found after death.

Injection into the bowels. Röhrig noted that a slow pulse or death invariably took place after the injection of cholalate of soda, and he thinks that the bile acids act as rapidly after injection into the rectum as into the blood vessels.[§] This is a matter of some interest in in the physiology of the bile.

Leyden injected several C.C. of 10 *per cent.* solution of bile acids into the rectum of two rabbits. Diarrhœa came on in both cases, and in one opisthotonos. Bile acids were recognised in the urine of both.[||]

A curious symptom was noted by von Dusch,[¶] Kühne,[**] and Feltz and Ritter,[††] and others during the injection of the acids into the vein; the creature thrusts out its tongue and licks its lips as if to free itself from some disagreeable taste. I have noted this appearance myself repeatedly. It is possible it may be due to the presence of the bitter bile acid salts in the blood.

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[*] Leyden, *op. cit.* p. 66.

[†] Röhrig, *Arch. d. Heilkunde*, 1863, p. 414.

[‡] Leyden, *op. cit.* p. 68.

[§] Röhrig, *loc. cit.*

[||] Leyden, *op. cit.* p. 67.

[¶] Th. von Dusch, *Untersuchungen und Experimente als Beiträg zur Pathogenese des Icterus*, Leipzig, 1854, p. 20.

[**] Kühne, *Arch. f. path. Anat.* 1858, Bd. xiv. p. 324.

[††] Feltz and Ritter, *Journal de l'Anatomie et de la Physiologie*, 1874, t. x. p. 576 *et seqq.*

Feltz and Ritter have also remarked an exaggeration of all the secretions, ptyalism, increased secretion of the mucus of the nose, abundance of urine, and loose stools. They look upon these symptoms as an effort of the œconomy to eject the poison. This is quite a possible explanation; but salivation and purging are so often seen in dogs after any drug that they can hardly be regarded as peculiarities of the action of the bile acids. Mr. Graham Brown noticed no salivation nor vomiting, and no diarrhœa, unless the dose were large, in rabbits under whose skin the bile acid salts had been injected.[*]

On the Red Blood Corpuscles. It is commonly said by the Germans that Hünefeld was the first to note that bile dissolved the corpuscles.[†] I have found, however, that this appearance was seen much earlier. Senac noticed that pus and bile, mixed with blood, lessened the red part of the blood.[‡] Portal plainly asserts that in experiments of his own he had seen that the bile mixed with blood dissolved the red globules.[§]

Hünefeld found that the blood, as soon as mixed with bile, became clear, and that the blood-corpuscles disappeared in a moment. The bile of man, oxen, dogs, pigs, cats, rabbits, hens, toads, frogs, and fish, had the same action upon the blood of men, pigs, and frogs;

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[*] Graham Brown, *Proceedings of the Royal Society of Edinburgh*, 1875, Vol. viii. p. 527.

[†] Hünefeld, *Der Chemismus in der thierischen Organisation*, Leipzig, 1840, p. 49.

[‡] Senac, quoted by Portal, *Obs. sur la nature et le traitement des mal. du foie*, Paris, 1813, p. 156.

[§] Portal, *op. cit.* p. 134, note. He quotes from his *Mémoires*, t. ii. p. 279, but I have not been able to verify this reference.

only the nuclei of the frog's blood corpuscles remained for a time unchanged, and then broke up into granules which at last disappeared. The bile of a still-born infant, which was free from bitterness, had none of this property. That of a man who died of a diabetes, very little.

On the other hand, Henle says that ox-bile is the best thing in the world in which to keep the red corpuscles of frogs; and remarks that Hünefeld has not taken note of the concentration of the bile.[*] Frerichs, too, says that the contents of the gall-bladder dissolve the red corpuscles less readily than does distilled water.[†] He is inclined, however, to admit that the salts of the bile acids may possess the property of dissolving the red corpuscles.

But most observers support the original statements of Hünefeld. The latest experiments on this matter, those of Koloman Müller, confirm them. Equal parts of filtered bile and blood were mixed, and though the decrease of the red corpuscles could not in all cases be at once detected, yet after a certain time, say an hour, it could always be noted, and in the end not a single corpuscle could be found.[‡]

After the discovery of the composition of the bile acids by Strecker, Theodor von Dusch was, as far as I can make out, the first to show that the solvent power of the bile upon the red corpuscles was due to the presence of the bile acids in this humour. Two or three crystals of glycocholate of soda were placed in a watch-glass with a drop of human blood; after a few minutes a transparent bright-red circle was found around the the crystal, which in 10 minutes had extended all over the fluid; under the microscope, no trace of the red corpuscles could be found. Taurocholate of soda showed the same property, but in a higher degree. With taurin itself, the blood-corpuscles were not dissolved, and this experiment has been confirmed by Koloman Müller.* Cholalate of soda gave the same appearances as glycocholate of soda.†

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[*] Henle, *Allg. Anat.* Leipzig, 1841, p. 430.

[†] Frerichs, *Klinik d. Leberkrankheiten*, Braunschweig, 1858, Bd. i. p. 100.

[‡] Koloman Müller, *Arch. f. exp. Path.* 1873, Bd. i. p. 222.

Kühne went a step farther, and examined the blood-corpuscles under the microscope at the moment that they were acted upon by the solution of the bile acids. He allowed the blood and the solution to run together under the covering glass. If a single red blood-corpuscle were kept under the microscope, it disappeared completely, without first losing its cupped shape, or increasing in size, or losing its definition.‡ I can fully support this statement of Kühne's as to the sudden and complete extinction of the red corpuscle when it touches the bile acid solution. I can only describe the appearance by saying that at one moment the red corpuscle is seen, and that, at the next, it is no longer there. It disappears without suffering any change in shape or colour. Traube compares it to the melting of snow in warm water;§ a comparison which I do not think good, as snow does not melt so rapidly as the corpuscle. The way in which distilled water or strong salt solution acts is so different that the destruction of the red corpuscle cannot be set down to the changes in the specific gravity of the fluid. In my own experiments I used a solution of bile acids 12 *per cent.* that is twice the strength of that of Kühne.

Kühne confirms the statement of von Dusch, that the salts of cholalic acid have the same action on the red corpuscles, and Kühne also finds that the same is true of choloidic acid.

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* Koloman Müller, *op. cit.* p. 224.

† Th. von Dusch, *op. cit.* pp. 13 *et seqq.*

‡ Kühne, *Arch. f. path. Anat.* 1858, Bd. xiv. p. 333.

§ Traube, *Berlin. klin. Wochenschrift*, 1864, p. 86.

The destruction of the red corpuscle is complete, and no membrane can be brought again into view by the action of iodine, or other colouring matter. But Kuehne finds that this is only true of the red corpuscles of mammals and birds. Though the bile of all vertebrates can dissolve the mammalian red corpuscle, yet the bile acids do not act upon the red corpuscle of frogs as they act upon that of mammals.[*] The disappearance is slower, the corpuscle changes its shape, but at last the whole of it becomes invisible. If, however, water be added, or better, solution of iodine, it becomes evident that the membrane of the corpuscle has not been dissolved for it is brought into view again.

On Leucocytes. Th. von Dusch declares that leucocytes are dissolved by bile,[†] a statement agreed to by Charcot.[‡] An increase of the white corpuscles in the blood of animals poisoned by the bile acids was noted by Leyden[§] and Mr. Graham Brown.[||]

On the Gases of the Blood. Feltz and Ritter found a slight decrease in the amount of oxygen contained in the blood of a dog poisoned by the bile acid salts, together with a slight increase in the amount of carbonic acid and nitrogen; and they found that blood which contained one and two *per cent.* of glycocholate of soda took up less oxygen and held more carbonic acid than blood which was free from glycocholates.[¶] The increase and decrease are, however, so small that they seem to me quite within the bounds of errors of estimation.

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[*] F. Simon (*Animal Chemistry*, Day's translation, London, 1845, vol. i. p. 106.) had noticed that the corpuscles of the frog were not very soluble in bile.

[†] Th. von Dusch, *op. cit.* p. 15.

[‡] Charcot, *Leçons sur les maladies du foie*, Paris, 1877, p. 75.

[§] Leyden, *op. cit.* p. 67.

[||] J. Graham Brown, *Proceedings of the Royal Society of Edinburgh*, 1875, Vol. viii. p. 520.

[¶] Feltz and Ritter, *Journal de l'Anatomie et de la Physiologie*, 1874, t. x. p. 587.

On the Liver Cells. Th. von Dusch first paid attention to the action of bile upon the liver cells. He came to the conclusion that bile, especially if concentrated, made the liver cells transparent and pale, and at last reduced them to a finely granular detritus.* But Kühne has shown that this solution of the cells is only apparent. Under the microscope it is true that the outline of the cell is lost, while apparently the contents are set free. But the contents do not separate from one another; and if the preparation be washed with water, the outline of the cells returns. In my own observations made in 1873, with the livers of freshly killed, healthy mammals, the bile taken from the gall bladder was added to the cells floating in saline solution, and the same appearances as those described by Kühne were seen. The cells lost their shape; they became rhomboidal, pale, and it was hard to make out the nucleus. The outline of the cell became altogether indistinct. Thus far the experiment seemed in favour of von Dusch's views. But the contents of the cells never became free. If made to move, they floated away and preserved the same relation to one another. Further, if acted on by iodine, the outline of the cell again came into view. Like changes in the cells were seen with a 12 *per cent.* solution of the bile acids.

Robin is also of opinion that the bile does not dissolve the liver cells.†

On the other hand, Kühne believes that this only holds good of the liver cells of mammals and birds. In the livers of frogs, taken in the spring, it could be seen that the outline became pale; and then, that the contents of the cell, which were made up of pigment and fine colourless granules, suddenly burst out, and followed the course of the stream. It is thus a very curious and noteworthy fact that the cells of the liver of the frog should dissolve in bile, while the red corpuscles resist.[*]

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* Th. von Dusch, *op. cit.* p. 36.

† Robin, *Leçons sur les humeurs*, Paris, 1867, p. 539.

On the glands and muscles. Like many other poisons, the bile acids cause a parenchymatous degeneration of the glands and muscles. Leyden[†] found this result in very many of the frogs, under whose skin 1. C.C. of a 10 *per cent.* solution of the bile acids had been injected. But it was not seen in all. I can testify to the accuracy of Leyden's observations on frogs, but I have not been able to see the same appearance in rabbits, probably owing to the short time that the poison was allowed to act, as Leyden found changes in two rabbits on whom the bile acids had been allowed to act at least twelve hours, but not in a third. Parenchymatous changes were also seen in dogs. Feltz and Ritter, too, found like changes in the liver and kidneys of dogs,[‡] Mr. Graham Brown in those of rabbits,[§] and Kemarsky in both of these animals.[||]

On striped muscles. As early as 1852, Budge made some experiments on this matter, and found that if frog's bile be laid upon the muscles of the frog's thigh, there followed a rapid contraction of the muscle; if the muscle had been cut into beforehand, there was a very marked contraction as a consequence of the irritation.[¶] Kühne also stated that bile acted as a marked excitant of muscles, whether applied to the nerves or direct to the muscles; and that the difference of observations was due to the varying degrees of concentration in the bile itself.[**]

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[*] Kühne, *op. cit.* p. 335.

[†] Leyden, *Beiträge zur Pathologie des Icterus*, Berlin, 1866, p. 60.

[‡] Feltz and Ritter, *Journal de l'Anatomie et de la Physiologie*, 1874, t. x. p. 575.

[§] J. Graham Browne, *Proceedings of the Royal Society of Edinburgh*, 1875, Vol. viii. p. 531.

[||] Kemarsky, Hofmann and Schwalbe's *Jahresberichte f.* 1875, p. 172.

[¶] Budge, Froriep's *Tagesber.* 1852, No. 475, p. 343.

[**] Kühne, *Arch. f. Anat. Phys. u.s.w.* 1859, p. 235.

Leyden found that, if the muscle of a frog be touched with a solution of bile acids, small fibrillary contractions are seen. If a strong solution be used, the spot touched becomes whitish and opaque, and the whole muscle somewhat contracted.[*]

The observations of Albers[†] on the muscles and nerves may be here passed by, as they are general experiments and prove nothing directly as to the muscles.

Johannes Ranke injected a 1 *per cent.* or a ·5 *per cent.* of solution of glycocholate of soda into the hind limbs of frogs, and found that the muscles became as hard as wood, and no longer gave tracings when acted on by electricity. On passing saline solution through the vessels of the limb, the muscles became much swollen and transparent. He concludes that the bile acids have a direct paralysing action on muscles; not a weakening action like carbonic acid. The swelling of the muscle after the injection of the saline solution, and failure of the washing out of the muscle to restore its function show that the muscle is changed in its chemical composition.[‡]

In this last sentence I quite agree with Ranke, and I believe that all the phænomena described by him and by Budge and Leyden may be explained on chemical grounds. In repeating Ranke's experiments, I noticed all the phænomena which he has described. There were the irregular contractions of the muscles of the limbs as the injection passed into them, rigidity and hardness immediately after the injection, and an absence of contraction on the application of electricity to the sciatic nerves. Knowing, however, that bile acids will coagulate albumen, as a 1 *per cent.* solution will cause turbidity in white of egg, it would seem that the appearances described by Ranke would be very fully explained by the chemical action of the bile acids upon the albuminous bodies of the muscle.

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[*] Leyden, *op. cit.* p. 97.

[†] J. F. H. Albers, *Arch. f. path. Anat.* 1862, Bd. xxiii. p. 582.

[‡] Johannes Ranke, *Arch. f. Anat. Phys. u.s.w.* 1864, p. 340; also *Tetanus*, Leipzig, 1865, p. 395. After injecting bile acids into the femoral artery of a dog towards the periphery, Leyden found the corresponding muscles stiff and hard to the touch, while the animal could not use the limb. After death on the third day, the muscular fibres showed a well-marked granular change. (*Beiträge zur Pathologie des Icterus*, Berlin, 1866, p. 82).

I was thus led to make a series of experiments in which the bile acids should not be immediately injected into the muscle, but should act by the natural process of absorption. The solution of the bile acids was injected into the lymphatic sac, or under the skin of frogs. The amount given varied from ·05 to ·3 grm. Twelve experiments were made; and in nearly all no change in the curve traced by the myograph could be detected after the injection of the bile acids, the observations beginning immediately after the injection of the bile acids, and lasting up to the time that the muscles would respond to any amount of electricity that I was able to bring to bear upon them.

The method used was as follows: the sciatic nerve was prepared, carefully avoiding all injury of blood-vessels; the tendon of the gastrocnemius was attached to a string, and separated from the heel. The frog was then put into a moist chamber, and the string attached to the *tendo Achillis* fastened to a telegraph lever writing on a revolving cylinder. The sciatic nerve was then irritated by means of electricity from a Du Bois-Reymond's coil; it was applied not oftener than once every minute, and only of such amount as to cause the muscle to contract. In the first two or three experiments the injection was given before the muscle was ready.

As samples of the others I detail two of these experiments.

Jan. 22nd. Excellent normal curves obtained. ·1 grm. of bile acids injected under skin of back. No change in the curves save that they grow smaller in height from 15 to 60 minutes after injection.

Feb. 2nd. ·3 grm. of bile acids injected under skin of back. No change in the normal curves from 19 to 92 minutes after injection.

Upon the heart. It has long been known that in some cases of jaundice the pulse becomes slow. But Röhrig deserves the credit of having been the first to point out that it was the action of the bile acids which caused the slow pulse; and that it was not the bile pigments or cholestearin.

He found that if a quantity not less than 2 C.C. of filtered ox bile were injected into the jugular vein of rabbits, a distinct decrease in the number of the heart beats, 7 or 8 in the 15 seconds, could be made out with the stethoscope. An injection of 6 C.C. of bile would bring down the pulse of rabbits to 27 or 30 beats: and by repeated doses, only 12 or 13 beats would be heard in two minutes, and death take place, due as Röhrig states to paralysis of the heart.

Röhrig found that the pigments and the cholestearin had no action on the pulse; neither had taurin nor glycocoll; the soda salts of glycocholic and taurocholic acid, on the other hand, had the same action as the bile had itself, and the soda salts of cholalic acid were still more active. It is thus seen that the active elements in the bile are the conjugate acids; and that it is the cholalic acid, not the basic glycocoll, nor the taurin, that is the agent of the slow pulse.

Röhrig further found that the slow pulse appeared when the *vagi* had been cut, and also that the frog's heart, when cut out and plunged in a solution of bile acids, beat a fewer number of times than when cut out and plunged in serum, or distilled water; and from these *data* he concluded that it was the ganglia of the heart and not the *vagi* that were acted on by the biliary acids.[*]

Landois asserts that the first action of the bile acids is to increase the number of the heart beats. It is true that many poisons have at first the action contrary to that for which they are best known. Landois used only very dilute solutions, such as 10 C.C. of a 2 *per cent.* solution of bile acids diluted with 90 C.C. of distilled water. He found that in frogs, rabbits, and cats, the first result of the injection of the bile or bile acids into the heart was an increase in the number of beats.[†]

Leyden noticed also in the cut-out heart of the frog an increase of the beats from 11 to 15, and even to 24 in the quarter minute.[‡] In my own experiments on the frog, I invariably noticed a slight rise, from 9 in the quarter minute to 10 or 11, and these experiments were made, without disturbing the heart, by the injection of bile acid solution under the skin.

Traube, however, considered that Landois was altogether wrong in saying that small doses of the bile acids increase the beats of the pulse, while large ones decrease them. The difference depends upon the state of the regulating system, whether it be in greater or less activity. If this system be active, there is seen after injection of the bile acids a lowering of the blood pressure with a considerable rise in the number of the pulse. If the activity of the spinal part of the regulating system be removed, then there is a decrease in the beats of the pulse. The bile acids when injected into the jugular vein at once meet with and destroy, or injure, a certain number of red corpuscles; then the

[*] Röhrig, *Arch. der Heilkunde*, 1863, p. 385. There is also an Inaugural Dissertation, *Ueber den Einfluss der Galle auf der Herzthätigkeit*, Leipzig, 1863, which I have not been able to see.

[†] Landois, *Deutsche Klinik*, 1863, p. 449.

[‡] Leyden, *op. cit.* p. 93.

blood containing these dissolved red corpuscles and the bile acids is quickly carried through the right side of the heart into the lungs. The red corpuscles being dissolved can no longer act as the carriers of oxygen, and the blood is brought by the pulmonary veins to the left side of the heart and distributed to the coronary arteries; this blood is incapable of exchanging oxygen with the muscular walls of the heart, and they are therefore injured, and in this way a slow pulse is seen.[*]

About the same time Johannes Ranke arrived at the conclusion, somewhat similar to that of Traube, that the bile acids have a paralysing influence upon striped muscular tissue. To the influence of the bile acids upon the muscular fibres of the heart the slow pulse is therefore due.[†]

The statements as to the cause of the slow pulse being thus so contradictory, I attempted a few years ago a research upon this subject, the results of which were laid before the Royal Society.[‡] The first element which it was necessary to eliminate was the influence of the *vagus;* and thanks to von Bezold's discovery, a ready means in atropine was at hand, by which the inhibitory function could be removed.

The heart of the frog lends itself very readily to all researches of this kind; if arranged in a Bowditch's apparatus, the circulation can be readily kept up for hours, if fed by serum; and if the aorta be connected with a manometer, the number and force of the pulsations of the heart can be easily registered.

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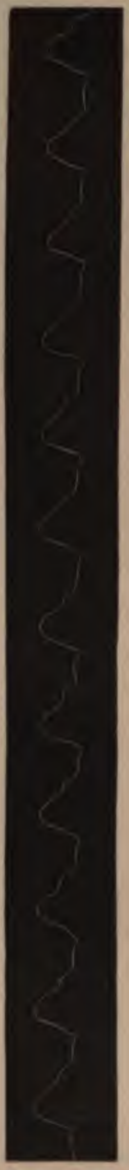
[*] Traube, *Berlin. klin. Wochenschrift*, 1864, p. 86, and *Gesammelte Beiträge*, Berlin, 1871, Bd. i. p. 366.

[†] Johannes Ranke, *Arch. f. Anat. Phys. u.s.w.* 1864, p. 340: also in *Tetanus*, Leipzig, 1865, p. 395. See his experiments above, p. 199.

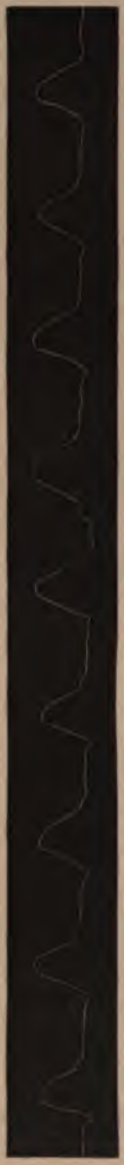
[‡] Wickham Legg, *Proceedings of the Royal Society of London*, 1876, Vol. xxiv. p. 442.

FIG. 1.



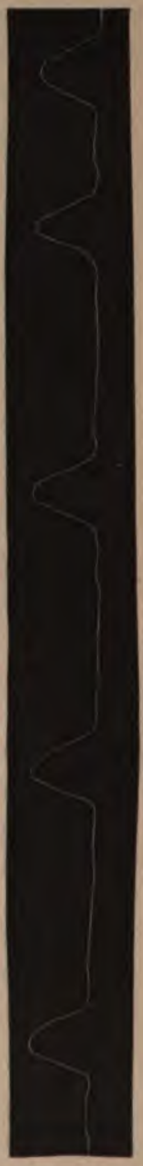
Normal tracing of frog's heart.

FIG. 2.



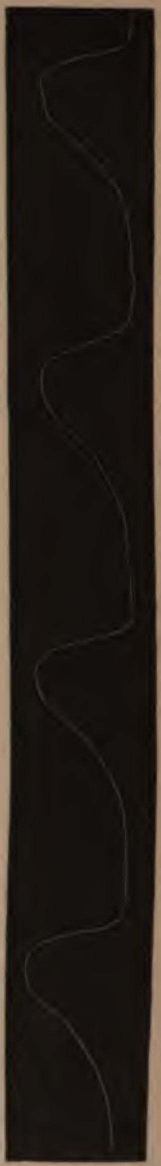
Tracing under influence of atropine.

FIG. 3.



First effect of the bile acid salts.

FIG. 4.



Later effect of the bile acid salts. (The cylinder having been reversed, the tracing must be read in a direction opposite to the other three).

FROG'S HEART IN BOWDITCH'S APPARATUS.

Time in Seconds.	Number of Pulsations.	Height of Curve in millimeters.	Remarks.
130	31	5·5	See Fig 1.
"	32	6	
"	38	4	Curves double topped.
"	31	6	Atropia introduced into the serum, so that it contained ·028 *per cent.* (See Fig. 2.)
120	24	7	Bile acids introduced into the serum.
"	16	7	Records in continuous 30 seconds. (See Fig. 3.)
"	16	8	Pulse now goes in pairs, 6·5 seconds between each pair of pulsations: between the pulses of each pair 3·2 seconds.
"	16	8·5	These do not go in pairs.
"	16	9	
"	16	8	These go in pairs.
130	13	12	A great change in character of curves. Systole reaches *maximum* height in 1·5 seconds. They slowly sink, scarcely meeting abscissa until the next contraction begin. They are nearly all alike. One takes up 23 mm. others 38 mm. (See Fig. 4.)
"	12·5	10	Immediately after the heart ceases to beat. No contractions upon electrical irritation.

Four other like experiments, with a like result, were made in December, 1872, and January, 1873. In one of them the bile acids were added to the serum first and the atropine added afterwards; but the same results were attained. The slowness of the pulse arose as before, and was unchanged by the addition of the atropine.

Another series of experiments on the irritability of the *vagus* was made.

The heart and right *vagus* of a frog laid bare, the heart beating 12 in 15 seconds. The *vagus* was then irritated by induced electricity and the heart stood still in diastole. Three or four drops of the solution of atropia of the British Pharmacopœia were now let fall upon the heart. After five minutes the beats were 7 in 15 seconds. The right *vagus* was then again irritated by induced electricity with no change in the heart. After 10 minutes, four drops of a 10 *per cent.* solution of bile acids were let fall upon the heart and neighbourhood. Thereupon, for nearly a minute, the heart beats rose to 10 in 15 seconds, but directly after fell to 6 in 15 seconds, the right *vagus* was again irritated but no change followed. Three minutes after, the beats were 5 in 15 seconds. The experiment was then broken off.

Two other experiments were made with like results. They would seem to show that the bile acids do not restore to the *vagus* the inhibitory power destroyed by the atropia.

With mammals I have attained like results.

If the inhibitory action of the *vagus* can therefore be excluded, there remain two other factors as a cause of the slow pulse, the muscular walls and the ganglia of the heart.

To deal first with the muscular walls, to the failure of which both Traube and Johannes Ranke attribute the slow pulse.

It has already been shown (p. 198.) that the bile acids have no physiological action upon striped muscular tissue, although they have a marked chemical action when injected into muscles. Have they, then, any chemical influence upon the ventricle? To test this supposition, I thought of making some experiments upon the action of the bile acids on the ventricle when separated from the rest of the heart.

It is commonly said that the ventricle of the frog's heart continues to beat for some time after it be severed from the auricles. I found, however, that the time was not long enough, nor the beating of the ventricle constant enough, to enable me to judge of the difference in time taken to bring the ventricle to a standstill if immersed in serum, or in serum containing 1 *per cent.* of bile acids. I fell back therefore on a method employed by Luciani* in Ludwig's Laboratory. It consists in introducing into the ventricle of the frog's heart, a tube divided vertically by a septum, and tying the ventricle on to the cannula below the auricles. The heart is supplied by serum through the double cannula and each pulsation is recorded by a manometer. I made five of these experiments, but I could detect no change in the alternate periods of rest and of contractions, as described by Luciani, after the introduction of bile acids in 1 *per cent.* into the serum, nor after the removal of the bile acid serum and the feeding of the heart with pure serum. Both before and after the use of the bile acids the contractions of the ventricle were alike. It would seem, therefore, that the bile acids have no action, either chemical or physiological, upon the ventricle of the frog's heart separated from the auricles.

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* Luciani, *Arbeiten aus dem phys. Anstalt zu Leipzig*, 1873, Jahrg. vii. p. 120.

If, then, the bile acids have no influence upon the ends of the *vagus* in the heart, nor upon the muscular tissue, there remains, in the present state of knowledge, only one other cause of the heart's movement which may beget a slow pulse; the ganglia of the heart. How these are affected by the bile acids there is no direct evidence to show. I do not know of any means by which these ganglia can be put out of play; and thus immediate proof that the ganglia are concerned is wanting. But if an argument, *per viam exclusionis*, be allowed, then it must be that the slow pulse is due to the action of the bile acids upon the cardiac ganglia.

I only became acquainted with the observations of J. Steiner a few months ago. He finds, as I do, that the slow pulse is not due to the excitement of the ends of the *vagus*, as the slow pulse appears after atropia has been given. But he has also made an observation of much interest. If bile be let fall upon the back surface of the frog's heart, there is at once a fall in the pulse, or even complete cessation of the heart's beats. But if the bile only touch the fore surface of the heart there is no change in the pulse for 10 minutes. Further, if the ventricle were cut off after Stannius' ligature were applied, the sinus still beat; but if touched with bile, the sinus at once ceased to pulsate. Again, if the Stännius' ligature were applied to the heart, the sinus taken away and the ventricle cut off, the auricle still beat, and continued to beat after it was touched with bile, though after some time the number of pulsations became less.

Steiner thinks that it is proved that the bile acts upon only one of the ganglia of the heart, that in the sinus, and not on the atrio-ventricular ganglia.*

On the hearts of snails. It has been asserted that the heart of the snail shows no nervous elements. I have made a number of experiments on the action of the bile acids upon the heart of this animal, but I have perceived no change worthy of note. The bile acids seemed to have no influence, neither increasing nor decreasing the number of pulsations, which are always very irregular.

On the lymphatic hearts of frogs. Röhrig has made some observations on the influence of the bile acids on the lymphatic hearts of the frog. Both hearts were laid bare, and six drops of a 5 *per cent.* solution of glycocholate of soda spread upon the muscular tissue. Before the bile acids, the number of beats was 12 in 15 seconds; one hour after, 10 beats; two hours, 8; three hours, 6; four hours, 4. At the end of four hours the least number of beats was attained, and at the end of six, the usual number was again seen.

Röhrig thinks that the action of the bile acids upon the lymph heart runs parallel with that upon the blood heart; though with small doses the lymphatic hearts may cease to act after a few hours, while the systemic heart is still beating, and the frog shows no change.†

My own observations lead to a conclusion altogether different from that of Röhrig. And perhaps I may be allowed to say that I somewhat regret my own results, as, if the bile acids had shown a distinct action on the lymphatic heart, it would have been an important aid to the proof that the cause of the slow pulse is nervous. I made six observations, and in no case found the rate of the pulsation of the lymphatic hearts changed soon after the administration of the bile acids by subcutaneous injection. The lymphatic heart only began to beat more slowly when general death was setting in from the action of the poison. The systemic heart, on the contrary, shows the action of the poison within a few minutes of its injection, and the pulsations may sink from 13 to 3 in the 15 seconds in seven minutes after the injection of 1 C.C. of a 10 *per cent.* solution of bile acid under the skin.

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* J. Steiner, *Arch. f. Anat. Phys. u.s.w.* 1874, p. 474.

† Röhrig, *Arch. d. Heilkunde*, 1863, p. 418.

I give the details of one experiment. On Dec. 24th. the right posterior lymphatic heart was exposed at 10.55 a.m. The pulsations vary from 7 to 9 in 15 seconds. At 11.5 the average is 9 in 15 seconds. At 11.5 one C.C. of a 10 *per cent.* of bile acids was injected under the skin of the neck.

11.12 a.m.	10 in 15 seconds.
11.15 ,,	9 ,,
11.20 ,,	9 ,,
11.24 ,,	struggles.
11.28 ,,	9 ,,
12 noon	10 ,,
12.20 p.m.	another injection.
12.25 ,,	11 in 15 seconds.
12.31 ,,	10 ,, ,,
Lymphatic heart now ceased to act.	
2 p.m.	animal found dead.

On the blood-pressure. Traube first called attention to the action of the bile acids on the blood-pressure. He found that if an animal be rendered motionless with woorara, and a bile acid soda salt be injected into the jugular vein, not towards the heart, but towards the head, the blood-pressure is much decreased and the pulse increased in frequency. If the dose of woorara have been large, the same results are obtained as those seen after division of the *vagi:* great decrease in the number of the pulse and in the blood-pressure. In both cases, however, there follows either an increase or a decrease of the frequency of the pulse; and, at the same time, a rise in the blood-pressure.

There is a great difference, too, according to the vessel into which the injection is made. An injection into the carotid will completely remove the effects of an injection into the jugular. For example, if the *vagi* be divided, and the bile acid salts injected into the jugular vein, there is a lowering of the blood-pressure and a decrease in number of the pulse. If, while the pulse and the pressure are sinking, another dose be injected into the carotid, the pulse and pressure at once begin to rise. If a similar experiment be made while the *vagi* are undivided, there are seen, after injection into the vein, lowering of the blood-pressure and increase in the number of the pulse; if, while these phænomena are still showing themselves, an injection be made into the carotid, there is increase of the blood-pressure and lowering of the pulse.*

Kemarsky found that, with animals under the influence of woorara, there was a fall in the blood-pressure. This fall is caused solely by the action of the bile acids on the heart, as if both *vagi* and spinal chord be divided the fall is still seen. If the *vagi* be not divided there is an increase in the number of the heart beats; if divided, the pulse becomes slow, so that Kemarsky thinks the slow pulse due to the action of the *vagus.*†

I have myself made some observations with the kymograph on the blood-pressure as affected by the injection of the bile acid salts into the blood; but in some respects I have not attained the same results as those of Traube.

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* Traube, *Berlin. klin. Wochenschrift*, 1864, pp. 86 and 147. Also in his *Gesammelte Beiträge*, Berlin, 1871, Bd. i. p. 366.

† Kemarsky, *Jahresberichte ueber die Fortschritte d. Anat. u. Phys. f.* 1875, Bd. iv. p. 171. Reasons for not accepting this conclusion of Kemarsky as to the *vagi* have been given above. (p. 205.)

April 30th. A middle-sized rabbit, kymograph in connexion with the carotid artery.

Time	Pulse in 15 seconds	Blood-pressure in millimeters
Normals	67 70 72	110 126 116
12. 59′ 50″ p.m. Injection of 1 C.C. of a 12 *per cent.* solution of Platner's crystallised bile into the external jugular vein towards the heart.		
1. 0′ 11″. Injection ended. From 12. 59′ 50″ to 12. 59′ 58″ there were 40 beats of the heart; from this time to 1. 0′ 11″ there were 52 pulsations, and the blood-pressure began to fall immediately.	71 65	108 78
1. 0′ 19″ ·6	61	84
1. 0′ 34″ ·6	58	90
1. 1′	62	94
1. 3′	68	106

In this experiment it will be seen that an injection of the bile acid salts into the jugular vein towards the heart was quickly followed by a fall both in the blood-pressure and the number of the pulse, though according to Traube there should be a fall in the pressure and an increase in the pulse.

In another experiment on a rabbit the only effect noted was an elevation of the blood-pressure slight and rapidly passing away.

April 28th. Black rabbit, large. Kymograph in connexion with carotid artery. Pulse not counted.

Time	Blood-pressure in millimeters
3. 25′	92
3. 28′	98

TIME		BLOOD-PRESSURE IN MILLIMETERS
3. 29′ 15″	Injection of 1 C.C. of a 10 *per cent.* solution of Platner's crystallized bile into the right external jugular towards heart.	98
3. 29′ 45″	Injection over	96
3. 20′ 55″		104
3. 30′		98
3. 30′ 45″		100
3. 32′		100
3. 33′		104
3. 34′		106

A clot now formed and the artery ceased to record.

In all the other experiments which I have made I have noticed a fall in the blood-pressure after the injection of the bile acid salts into the jugular vein. I have been somewhat surprised at the little effect which one, two, and three C.C. of a ten *per cent.* solution of bile acid salts, have when injected into the jugular. On the other hand, the same dose injected into the carotid causes at once marked symptoms, with a considerable rise in the blood-pressure. The blood-pressure sinks during the injection, but at once begins to rise somewhat irregularly and keeps high for a few seconds. It then falls, and comes to an end with the death of the rabbit.

The peculiar symptoms seen on injection into the carotid are described immediately below.

On the Respiration. A very curious appearance after the injection of the bile acids into the carotid was first noticed by Traube; a spasm of the respiratory muscles takes place, and the diaphragm is held in deep inspiration. Apnœa follows, but the heart still beats. If artificial respiration be practised, the animal can be kept alive. If only small doses be given, there is a great fall in the number of respirations, even to 2 in a minute.* Leyden has repeated these experiments.†

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* Traube, *Berlin. klin. Wochenschrift*, 1864, p. 147. Also in *Gesamm. Beiträge*, Berlin, 1871, Bd. i. p. 378.

† Leyden, *Beiträge zur Pathologie des Icterus*, Berlin, 1866, p. 70.

The inspiratory spasm is very well marked, as I can testify from my own observations; and it persists in the rabbit even after the removal of all the cerebrum above the tentorium, except the *corpora quadrigemina*. After their removal, the spasm is no longer well marked.

Mr. Graham Brown found that the respirations of rabbits were perceptibly decreased in rapidity after the injection of the bile acids under the skin.[*] Albers noted, 20 minutes after pure glycocholic acid had been placed under the skin of frogs, that the breathing was quicker; later on dyspnœa.[†]

On the Nervous System. It has already been noted that epileptiform convulsions, and tetanus have followed the injection of bile, even if filtered, into the veins. The same phænomena have followed the injection of the pure bile acid salts. It is thus probable that the bile acids in the filtered bile are the active agents in causing the nervous symptoms.

Theodor von Dusch noted these tetanic symptoms and opisthotonos, followed by sudden death, after the injection of solutions of glycocholate of soda and of taurocholate of soda into the jugular vein. A large amount, 8 and 16 C.C. of a 20 *per cent*. solution of glycocholate of soda, could be injected into the *vena saphena* of a dog without causing more than passing symptoms. After death, the lungs were found full of hæmorrhages, the right side of the heart filled with clotted blood; the left empty; while the *vena cava inferior* was distended with blood.[‡] Similar observations, though less minutely detailed, have been recorded by nearly every other observer who has experimented with the bile acids, such as Frerichs,[*] Kühne,[†] Leyden,[‡] Feltz and Ritter.[§]

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[*] J. Graham Brown, *Proceedings of the Royal Society of Edinburgh*, 1875, vol. viii. p. 527.

[†] J. F. H. Albers, *Arch. f. path. Anat.* 1862, Bd. xxiii. p. 582.

[‡] Th. von Dusch, *Untersuchungen und Experimente also Beitrag zur Pathogenese des Icterus*, Leipzig, 1854, pp. 18 *et seqq*.

At the time at which Theodor von Dusch wrote, the doctrine of thrombosis of the pulmonary artery was less widely spread than at present, and it is hardly surprising that he failed to draw the conclusions, which now seem to lie on the surface. Johannes Ranke and Baldauf, indeed, apparently without being acquainted with Theodor von Dusch's observations, have come to the conclusion that the sudden death is due to thrombosis of the pulmonary artery.[||] The blueness of the lips, the tetanic convulsions, the expulsion of the urine and fæces, after death the distension of the right side of the heart and the vessels leading into it, the right side being sometimes filled with clots,[¶] the pulmonary hæmorrhages, and the emptiness of the arteries, all noted by von Dusch, make the case a typical one of death from pulmonary embolism. The explanation which Johannes Ranke gives of the formation of the thrombosis is very probable. The bile acids dissolve the red corpuscles; as a consequence of the solution of the red corpuscles, a clot immediately forms, which is carried to the heart or into the pulmonary artery. And this explains the fact noted by Th. von Dusch that when the injection was made into a vein at a distance from the heart, such as the crural or saphena, sudden death did not always take place.[**] Johannes Ranke found after the same experiment that the vena cava, as high as the liver, was filled with a thrombus, while many of the smaller branches of the pulmonary artery were also filled with clots.

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[*] Frerichs, *Klinik d. Leberkrankheiten*, Braunschweig, 1858, Bd. i. p. 404.

[†] Kühne, *Arch. f. path. Anat.* 1858, Bd. xiv. p. 326.

[‡] Leyden, *op. cit.* p. 72.

[§] Feltz and Ritter, *Journal de l'Anatomie et de la physiologie*, 1874, t. x. p. 571.

[||] Johannes Ranke, *Die Blutvertheilung und der Thätigkeitswechsel der Organe*, Leipzig, 1871, p. 164.

[¶] Th. von Dusch says that he found a thrombus in a large pulmonary vein (p. 21). This is probably an error of observation for pulmonary artery.

[**] See the older observations with this same result, p. 118.

Johannes Ranke states that the dose of the bile, or the bile acid salts, which is enough to cause death in rabbits, is only fifteen milligrammes. I do not think that this is always the case. I have injected 50, 200, and even 800 milligrammes of Platner's crystallized bile in 10 *per cent.* solution into the jugular veins of rabbits, in different individuals, without causing thrombosis of the pulmonary artery or of the right heart. No obvious effect was caused by the injection of 50 or 200 milligrammes. But after the dose of 800 milligrammes, the pulse and respiration at once fell, and the rabbit appeared to be dying; it was killed at once by opening the chest; the heart was found still feebly contracting on the right ventricle and auricle; but none on the left side. Irritation of the ventricles with Pulvermacher's forceps called forth no contractions; but the same irritation to the phrenic nerve caused violent contractions of the diaphragm. Direct irritation of the muscles of the thigh, and of the anterior crural nerve was followed by marked contractions. Heart and pulmonary artery followed with a fine pair of scissors, but no clots were found. Urine from the bladder was turbid and straw-coloured, but showed no reaction with nitric acid.

Probably the difference in observation is due to a difference in the food of the animals; and the difference between the older experiments spoken of above, must be explained on the same grounds, or a difference in the constitution of the blood.

Huppert injected 3·3 grm. of glycocholate of soda, dissolved in 20 C.C. of water, into the jugular vein of a dog, and found that the creature, up to that moment very restless, became quiet, and fell into a sleep from which he could hardly be aroused.* In the same way,

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* H. Huppert, *Arch. d. Heilkunde*, 1864, p. 241.

Mr. Graham Brown noticed much drowsiness, ending at last in coma, after the injection of the bile acids under the skin of rabbits. No convulsions were noticed; nor did the pupil show any change.* Albers speaks of convulsions and other nervous symptoms, after pure glycocholic acid had been introduced under the skin of frogs.† Leyden does not think that the bile acid salts are a direct irritant. When the sciatic nerve of a frog with the muscles still attached to it was laid in bile, no contractions of the muscles appeared.‡ I have no doubt of the action of the bile acid salts as narcotics. When moderate doses are given to frogs, the animals shortly become torpid, insensible to all stimulus, showing no reflex action whatever. They lie, with contracted pupils, as if in a deep sleep.

I have made some observations upon the changes in the reflex movements which follow the administration of bile acid salts. Out of five experiments, nearly all alike, I give the details of one.

Dec. 19. The anterior cerebral hemispheres of a frog were removed, the optic thalami being left uninjured. The foot of the frog was irritated by being plunged in water, made just perceptibly acid to taste by sulphuric acid.

The numbers represent the time in seconds which passed between the plunging of the foot into, and its withdrawal from, the water with which it was irritated.

12.22 p.m. 12, 6, 7, 8, 6, 7, 6.

12.32 p.m. ·5 C.C. of a 10 *per cent.* solution of bile acids injected under the skin of the back.

12.39 p.m. 1, 2, 1, 1, 29, 27, 15, 16, 21, 28, 22, 26.

1 p.m. The head was cut off.

1.25 p.m. 9, 9, 9, 9, 10, 10, 10.

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* J. Graham Brown, *Proceedings of the Royal Society of Edinburgh*, 1875, Vol. viii. p. 530.

† J. F. H. Albers, *Arch. f. path. Anat.* 1862, Bd. xxiii. p. 582.

‡ Leyden, *Beiträge zur Pathologie des Icterus*, Berlin, 1866, p. 95.

In all cases a minute passed between the application of the irritant; and the foot was well washed with distilled water after each observation.

It would appear that the reflex irritability is decreased by the action of the bile acids; a statement in which Kemarsky also joins.[*]

Upon the serous membranes. It is well known that an escape of bile into the peritonæum is an almost fatal accident, peritonitis being at once set up. This property of the bile would seem to be due to the presence of the bile acid salts, as the same violent peritonitis follows the injection of these salts into the peritonæum.

On the temperature. Röhrig was struck by the coldness of the animals poisoned by the bile acid salts, and found their temperature much lower than natural.[†] Feltz and Ritter also speak of a low temperature as a result of poisoning by the bile acids.[‡] Kemarsky found the temperature to be lowered in direct proportion to the amount of bile acid salts injected into the blood; an inconsiderable rise of temperature preceded the fall.[§] Huppert, in two dogs, found very little change;[‖] the thermometer in the rectum being constant at 37°·6 C. or 37°·8 C. (99°·6 F. or 100° F.)

Röhrig goes so far as to propose the bile acids as a remedy in fever to bring down the temperature. It is possible, however, that the lowering of the temperature is not due to a specific action of the bile acids, for many poisons cause a fall in the temperature some hours before they put an end to life.

On the Urine. After the injection of the bile acid salts into the blood, the urine quickly becomes high-coloured from the presence of hæmoglobin. No red blood corpuscles can be found, but abundance of casts of the urinary tubules, with dark granules. So far all observers are agreed. But Frerichs announced that in the urine is also to be found bile pigment; and he explains the presence of the bile pigment by a metamorphosis in the circulation of the colourless bile acid salts into pigment.[*] Kühne found bile pigment in the urine after the injection of bile acids into the circulation, but apparently attributed the presence of the pigment to the setting free of hæmoglobin into the plasma.[†]

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[*] Kemarsky, *Jahresberichte ueber die Fortschritte d. Anat. u. Phys. f.* 1875, Bd. iv. p. 171.

[†] Röhrig, *Arch. d. Heilkunde*, 1863, p. 394.

[‡] Feltz and Ritter, *Journal de l'Anatomie et de la Physiologie*, 1874, t. x. p. 576.

[§] Kemarsky, *Jahresberichte ueber die Fortschritte d. Anat. u. Phys. f.* 1875, Bd. iv. p. 171.

[‖] H. Huppert, *Arch. d. Heilkunde*, 1864, p. 241.

I have myself been unable, in numerous experiments, to satisfy myself of the presence of bile pigment in the urine of rabbits after the injection of the bile acids into the blood. I am inclined to believe that the difference in observation is due to the animals experimented upon. The urine of dogs often shows a Gmelin's reaction, when the animals are believed to be in perfect health.

Mr. Graham Brown records the appearance of albumen and bile pigments in the urine of rabbits, as a rare event, after bile acid salts have been injected under the skin.[‡]

The same observer noted the presence of red blood corpuscles once or twice in the urine; but the spectrum did not show the characteristic absorption bands of blood on the two occasions when the test was applied. This is another instance of the difference in the effect caused, according as the poison is injected into the blood, or under the skin.

Mr. Graham Brown found in nearly every case a great rise in the amount of nitrogen excreted by the urine immediately after the injection of the bile acid salts under the skin; in one case the amount passed in the first 24 hours after the injection was just double the average of the three foregoing days.

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[*] Frerichs, *Klinik d. Leberkrankheiten*, Braunschweig, 1858, Bd. i. p. 404. See also *Arch. f. Anat. u. Phys*, 1856, p. 59, note.

[†] Kühne, *Arch. f. path. Anat.* 1858, Bd. xiv. p. 324. See also his *Lehrb. d. phys. Chemie*, Leipzig, 1866, p. 89.

[‡] Graham Brown, *Proceedings of the Royal Society of Edinburgh*, 1875, Vol. viii. p. 528.

Feltz and Ritter made two observations with the taurocholate of soda, but whether it were injected under the skin of the dog or into the veins does not appear. They noted a slight increase in the amount of nitrogen, but it was so slight that it might be quite within the physiological boundaries; and the urea was markedly decreased and the uric acid increased.[*] The urine seems in most cases to be alkaline.

PHYSIOLOGICAL ACTION OF THE DERIVATIVES OF THE BILE ACIDS.

Cholalic acid. It was noticed, as early as 1854, by Theodor von Dusch that cholalate of soda dissolved the red corpuscles as readily as the glycocholate,[†] and Röhrig found that the pulse became more rapidly slow when cholalate of soda was injected into the veins, than when the bile acid salts themselves were used.[‡]

Hoppe-Seyler, also, saw most severe symptoms follow the injection of two grammes of the same salt into the jugular vein of a dog. The urine, much decreased in quantity, held blood-colouring matter and albumen. There were vomiting and diarrhœa, and in two days the animal was dying. After death many hæmorrhages were found in the intestines which held little else but blood and bile. The kidneys on section looked quite black; and the tubules were filled with blood crystals.[§]

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[*] Feltz and Ritter, *Journal de l'Anatomie et de la Physiologie*, 1874, t. x. p. 585.

[†] Th. von Dusch, *Untersuchungen und Experimente als Beitrag zur Pathogenese des Icterus*, Leipzig, 1854, p. 15.

[‡] Röhrig, *Arch. d. Heilkunde*, 1863, p. 397.

[§] Hoppe-Seyler, *Arch. f. path. Anat.* 1862, Bd. xxv. p. 183.

Feltz and Ritter came to conclusions quite different from those of observers who have gone before them; so different that it would almost appear that they experimented with a body differing in chemical composition. They find cholalate of soda much feebler in its action than the glycocholate and the taurocholate; the doses require to be much larger to produce the same appearances. They have never seen any blood in the urine and only by accident any colouring matters. The blood also does not appear to be changed.*

I should myself feel inclined to put greater trust in the observations of Röhrig and Hoppe-Seyler on the action of cholalic acid, than in those of Feltz and Ritter. For it would be a strange thing if a body which is the foundation of the bile acids, and allied to them in so many chemical and physical properties, should prove as inert, as Feltz and Ritter found it, in its physiological properties.

Choloidic Acid (Demarçay). Feltz and Ritter saw no perceptible changes follow the injection of two grammes of the soda salt of this acid into a dog weighing 5·750 kilogrammes†

Kühne states that the red corpuscle is dissolved by choloidic acid.‡

Dyslysin. This body, dissolved in cholalate of soda, was injected into a dog by Feltz and Ritter in doses of two grammes. No symptoms whatever were noticed.§

Glycocoll. All observers who have made observations with this body have stated that it is harmless to the animal œconomy.‖ Schultzen and Nencki found a great increase in the urea, corresponding to the amount of nitrogen in the glycocoll, after feeding animals with this body; but it does not appear to have acted in any way as a poison.[*]

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* Feltz and Ritter, *Journal de l'Anatomie et de la Physiologie*, 1875, t. xi. p. 148.

† Feltz and Ritter, *loc. cit.*

‡ Kühne, *Arch. f. path. Anat.* 1858, Bd. xiv. p. 333.

§ Feltz and Ritter, *loc. cit.*

‖ Röhrig, *op. cit.* p. 396. Feltz and Ritter, *op. cit.* p. 151.

Taurin. Neither is taurin endowed with any very active physiological gifts. Nearly all observers look upon it as inert.[†] Salkowski, however, found that rabbits were somewhat sensitive to its use, much more so than dogs or men. When given by the mouth, the greater part of the taurin reappears in the urine of rabbits; there is four or five times as much sulphuric acid as natural; and it is to the waste of alkali that Salkowski attributes the injurious action of taurin.[‡]

PHYSIOLOGICAL ACTION OF THE BILE PIGMENTS.

Röhrig appears to have been the first to make experiments with the bile pigments. He found that saturated solutions, in soap, of cholepyrrhin (bilirubin) and of bilifulvin, injected into the circulation in doses of 6 to 8 C.C. had no influence on the action of the heart.[§]

Feltz and Ritter found that the bile pigments had no marked action on the animal œconomy. The injection of bilirubin was followed by an obstinate constipation, and an increase in the amount of urine in which bilirubin could be readily detected. The writers note much the same appearances after the injection of biliprasin, bilifuscin, and bilihumin.[¶]

To sum up, it may be stated that the bile pigments are physiologically inert.

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[*] Schultzen and Nencki, *Zeitschrift f. Biologie*, 1872, Bd. viii, p. 124.

[†] Th. von Dusch, Röhrig, and Feltz and Ritter, *locis citatis*; Koloman Müller, *Arch. f. exp. Pathologie*, 1873, Bd. i. p. 233:

[‡] Salkowski, *Berichte der deutschen Chemischen Gesellschaft zu Berlin*, 1872. Jahrg. v. p. 637. See an abstract by himself of his work in Virchow and Hirsch's *Jahresbericht f.* 1873. Bd. i. p. 159.

[§] Röhrig, *op. cit.* p. 400. Cf. p. 86. of this work,

[¶] Feltz and Ritter, *op. cit.* p. 154.

Physiological Action of Cholestearin.

Dr. Austin Flint, the younger, first called attention in 1862[*] and again in a pamphlet published in the French language at Paris in 1868[†] to the physiological action of cholestearin. He first attempts to prove that this body is an excremental matter formed by the metamorphosis of the brain and excreted by the liver. In the upper part of the intestine, the cholestearin is changed into a body called stercorin. This is then cast out of the body and forms a most important element in the excretions of the body. If the liver do not act properly, if there be suppression of its secretion, then the cholestearin is retained in the blood and acts as a poison. This pathological state Dr. Flint calls cholestearæmia, and to it the nervous symptoms seen in jaundice may be set down.

It may be noted that Dr. Flint made no direct experiments with cholestearin upon animals. His experiments are a series of estimations of the amount of cholestearin in the blood. The trouble and uncertainty which attend all estimations of bodies in the blood are well known; and it has struck me in looking down the figures given by Dr. Flint that in very many cases the amount of cholestearin found varies inversely with the amount of blood submitted to examination. Where a larger amount of blood has been examined, a smaller percentage of cholestearin has been found, and *vice versâ*.

The views of Dr. Flint have not met with universal acceptance; and attempts have been made to test their value by directly injecting cholestearin into the blood. A difficulty, however, arises from the insolubility of cholestearin in the ordinary fluids indifferent to the blood. Koloman Müller made a sort of emulsion by first finely rubbing up the cholestearin with glycerine, and then adding solution of soap. A thick emulsion was thus got in which the cholestearin was very finely divided, 8. C.C. holding 45 milligrammes of cholestearin. This emulsion of cholestearin was injected into the veins of about 9 dogs, and the injection was followed by coma, and death. Koloman Müller concludes that the nervous appearances seen in jaundice are due to the accumulation of cholestearin in the blood.*

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[*] Austin Flint, jun. *American Journal of the Medical Sciences*, 1862. vol. xliv. p. 305.

[†] *Recherches exp. sur une nouvelle Fonction du Foie*, Paris, 1868.

It would be worth seeing if the nervous symptoms described by K. Müller follow an injection of the same emulsion under the skin. It seems very likely that a thick emulsion injected into the veins would be followed by severe symptoms, not to be all set down to the physiological action of cholestearin.

On the other side are the experiments of several observers. Pagès, the year after Dr. Austin Flint published his pamphlet in French, made cholestearin the subject of his inaugural thesis. He apparently made his experiments under the direction of Feltz and Ritter. The first experiments were not likely to give any information, as the cholestearin was dissolved in æther, and æther is a fluid to which the blood is by no means indifferent. In the last two experiments he attempted to dissolve the cholestearin in soap. Koloman Müller says that he was unable to obtain a true solution with soap. Be this as it may, 25 milligrammes of cholestearin injected into the veins caused no symptoms whatever. Pagès thinks that whatever symptoms are caused by cholestearin are due to its solid particles acting as emboli.†

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* Koloman Müller, *Arch. f. exp. Pathologie*, 1873, Bd. i. p. 213.

† Henri Pagès, *De la cholestèrine et de son accumulation dans l'économie*, Thèse de Strasbourg, 1869. These experiments have been republished by Feltz and Ritter, *Journal de l'Anatomie et de la Physiologie*, 1875, Année xi. p. 166.

A Russian observer, M. Chomjakow, chose oil of almonds as a vehicle. A 5 *per cent.* solution in this oil retained its transparency at 37° to 40° C. 7·5 C.C. of the solution, corresponding to 345 milligrammes of cholestearin, were injected into the veins of cats. The following were the results: either the animals underwent the injection without any symptoms at all, or death followed immediately upon the injection either of cholestearin in solution or of almond oil alone. In this case the cause of death was infarction of the pulmonary artery.*

V. von Krusenstern, in O. Liebreich's laboratory at Berlin, came to precisely the same result as Chomjakow, but with a different solvent. With a 3 *per cent.* solution of stearin soap he made a 0·5 *per cent.* solution of cholestearin. The daily injection of this solution (10 to 90 C.C. =5 to 45 milligrammes of cholestearin), into the veins of dogs caused not the least change in their state.†

Looking upon these experiments and comparing them with those of Koloman Müller, it will be hard to come to any other conclusion than that cholestearin is a harmless body, the injection of which into the veins is followed by no evil results. If this position be granted, the theory of a cholestearæmia must fall.

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* M. Chomjakow, *Kriegsmedicinische Zeitschrift* (Russian) 1872. Quoted by V. von Krusenstern, *Arch. f. path. Anat.* 1875, Bd. lxv. p. 412.

† V. von Krusenstern, *op. cit.* p. 418.

CHAPTER X.

THE ETYMOLOGY, HISTORY, AND ÆTIOLOGY OF JAUNDICE.

JAUNDICE signifies a yellowness of the skin. It comes from the French word *jaune*, yellow. The Greeks called the disease *icterus*. Of this word Aretæus says: "it is derived from certain four-footed and terrestrial animals, called ἰκτίδες whose eyes are of this colour."[*] Pliny the elder, on the other hand, says there is a bird called icterus, the sight of which was cure to the jaundiced patient, but death to the bird.[†] Aretæus is, no doubt, right. The disease must have had a name before a means for its cure was described: and the Greeks were in the habit of keeping these ἰκτίδες for the same purpose as we do cats,[‡] so that the source of comparison would be at hand.

Suidas derives the word icterus from ἰκτῖνος, a kite:[§] because, says de Haen,[||] they also have jaundiced eyes.

The Latins called jaundice *morbus regius*, from the yellow colour of gold, the *Rex metallorum*, and not from the royal diet or regimen which was believed to be good for the patient.[*] For the same reason, another Latin synonym is *aurugo*, or *aurigo* from *aurum*, gold. Also *morbus arcuatus*, *seu arquatus*, from the circles seen by the jaundiced.[†]

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[*] Aretæus, *On the Causes and Symptoms of Chronic Diseases*, Bk. i. chap. xv. Adams' trans. Syd. Soc. 1856, p. 326.

[†] C. Plinii Sec. *Nat. Hist.* Lib. xxx. Cap. xi. Lugd. Bat. 1669, t. iii. p. 321. This bird was called *galbula* or *galgula* by the Romans, and is supposed to have been the golden oriole.

[‡] Dr. Rolleston (*Journal of Anat. and Phys.* 1868, Vol. ii. p. 47) is of opinion that the ἴκτις performed the same office in Greek houses as the *felis domestica* in ours, viz. that of killing mice. The ἴκτις appears to be the yellow-breasted marten; and not a ferret, as some writers state.

[§] Suidas, *Lexicon*, t. ii. ed. Kuster. Cantabrig. 1705.

[||] De Haen, *Prælectiones*, Viennæ, 1780, t. ii. *Tract. de vermibus, etc.* p. 108. Villeneuve gives also another derivation: "quelques-uns font dériver la dénomination dont il s'agit d' ἴκτις, ἰκτῖνδος, *(sic)* espèce de mouches de bois dont les yeux sont de couleur jaune." (*Dict. d. Sci. méd.* Paris, 1818, t. xxiii. p. 386.)

By the Germans, jaundice is called *Gelbsucht*, although of late years the growing custom of using words of a non-Teutonic source has made this excellent name give way almost entirely to icterus. By the French, *jaunisse* is almost forgotten, or thought vulgar, and *ictère* is always used.

Jaundice could hardly fail to be noticed early in the history of mankind, as the change of complexion and colour would be a striking appearance. Accordingly there is abundant mention of it in the genuine Hippocratic writings, which most often speak of it as a complication of other diseases, chiefly fevers. In the *Aphorisms* it is said to be a bad sign if the liver become hard during a jaundice; and in the third book of the *Epidemics*, that an habitual pain in the neighbourhood of the liver, with other symptoms, preceded a jaundice.[‡] It may be disputed if the father of medicine conceived any relation between the bile secreted by the liver and the symptom of jaundice. In the other books of the Hippocratic Collection it is said that the deep yellow colour and the white colour come from the liver or disease of the liver: and in these states, the jaundices, dropsies, and leucophlegmasiæ which come from the liver are whitish, while those from the spleen are more dark.[*] Another white jaundice is spoken of as coming from phlegm, and attacking chiefly in the winter. Its colour is white, and the chest is filled with phlegm. The urine is white and thick.[†] This certainly does not correspond to what we call jaundice, nor does the second kind of jaundice described just before by the same writer. The first and the third are more like the symptom as we speak of it to-day. The first kind is caused by the bile being put in movement, and being fixed in the skin and head,[‡] so that the body is as yellow as a pomegranate. The eyes are yellow, the stools white and stinking. It will be seen that some caution must be used when early writers speak of ἴκτερος for they do not always mean the same as we do; and like confusion has been seen almost in our own day.

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[*] Celsus, *Medicin.* Lib. iii. cap. xxiv. "Per omne vero tempus utendum est exercitatione, frictione: si hiems est, balneo; si æstas, frigidis natationibus; lecto etiam et conclavi cultiore, lusu, joco, ludis, lascivia per quæ mens exhilaretur: ob quæ regius morbus dictus videtur." Others may think that as mental worry predisposes to jaundice, so it is called the royal disease from the anxieties of court life. It is not every one who can have the stoical virtue of Antoninus and say: "Even in a palace, life may be led well."

> I have been told the very place transforms men,
> And that not one of a thousand, that before
> Lived honestly in the country on plain salads,
> But bring him thither, mark me that, and feed him
> But a month or two with custards and court cake-bread,
> And he turns knave immediately. I'd be honest;
> But I must follow the fashion, or die a beggar.
>
> MASSINGER: *Great Duke of Florence*, I. i.

[†] Paracelsus is said to have called jaundice *morbus luseoli* from the salt which he administered in these cases; but in his writings he seems to me to have very frequently used the word *icterus* or *icteritia*.

[‡] Hippocrates, *Aphorism.* Sect. vi. § 42, and *Epidem.* lib. iii. 13th patient, case of Apollonius of Abdera. Littré's ed. t. iv. p. 574, and t. iii. p. 138.

Galen also asserts that the yellow bile, when it is carried all over the body, still keeping its own nature, causes a disease called jaundice.[§] Aretæus says much the same thing, adding, however, that jaundice may arise from the stomach, spleen, kidneys, and colon, and is not solely formed from the liver as some have supposed.[‖] The jaundice caused by the liver is brought about in this fashion: if the liver and gall bladder continue to secrete bile, but the passages which convey the bile to the intestine be obstructed, the bile regurgitates; it therefore becomes mixed with the blood, and the blood passing over the whole system carries the bile into every part of the body, which acquires the appearance of bile. It would be hard to express in different language the doctrine of jaundice from absorption, now universally held.

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[*] *Epidem.* Lib. ii. Sect. i. Cap. x. Littré's ed. t. v. p. 83.

[†] *De aff. int.* Cap. xxxviii. Littré's ed. t. vii. p. 261.

[‡] The same view of the pathology of the disease is taken by the writer *de affect.* (Cap. xxxii. Littré's ed. t. vi. p. 245.)

[§] Galen, *De med. method.* Lib. ii. Cap. i. Kühn's ed. Lips. 1826, Vol. xi. p. 74.

[‖] Aretæus, *On the Causes and Symptoms of Chronic Diseases*, Bk. i. Chapter xv. Adams' translation, p. 324.

Aëtius gives the views of Galen and Ruffus; he says: Jaundice is an effusion of bile all over the body. They err who think that in all cases of jaundice the liver must be diseased. Sometimes a jaundice is caused by weakness of the gall bladder, which does not draw to itself the bile out of the liver, as it accustomed, and thus leaves the blood impure.[*] Paul teaches that jaundice is a diffusion of the bile all over the body, sometimes of the yellow, sometimes of the black, bile. Jaundice with fever would seem to be caused by a hot inflammation of the liver which renders the blood bilious. A jaundice without fever is caused by an affection of the gall bladder and its ducts.[†]

With Paul the list of the Greek and Latin writers ends, and the Arabians, to whom medicine and civilisation are so much indebted, give us a physiology but little different from that of the classical writers.

Amongst the dreams of Paracelsus will be found the statement, apparently as a reaction against the humoral pathology, that the bile never causes any disease. Jaundice is not due to the bile but to the union of three salts, "*sal entalicum, sal vitriolatum, et liquor sulphuris resoluti.*"[‡]

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[*] Aëtius, *Tetrabibl.* III. serm. ii. cap. xvii. Basil. 1542, p. 582.

[†] Paul of Ægina, Book iii. Cap. L. Adams' trans. Vol. i. p. 580. See p. 582 for a general view of the classical writers.

[‡] Paracelsus, *Opera*, Genevae, 1658, Vol. i. p. 486. De Icteritiis. It would seem very doubtful, more so than in the case of the classical writers, what Paracelsus meant by *icteritia*. He indeed begins this book with: "Icterus sive icteritia,"

Sylvius de le Boe denies that obstruction in the bile ducts is an efficient cause of jaundice.* He points out that in some cases of jaundice, which he has dissected, he had found no obstruction; and further, that in some cases the stools were coloured, or but little less coloured than usual. With this writer, an important age, not merely in the history of jaundice, but in that of medicine at large, is reached. It is the time of the discovery of the circulation by Harvey, of the lacteals by Aselli, and of the thoracic duct by Pecquet. With the changes in physiology, changes in pathology likewise appear. The history of jaundice must now be broken up into three heads: i. a theory which attributes the symptom of jaundice to changes in the blood and its colouring matter, thence called hæmatogenous jaundice: ii. a theory which makes the bile to be merely separated by the liver from existing elements in the blood, not truly secreted by the liver; jaundice may thus arise when the liver ceases to excrete the bile, the elements of which accumulate in the blood and cause the general yellow appearance: iii. a theory which attributes the phænomena of jaundice to the absorption into the mass of the blood of bile already formed. Under these three heads all prevailing doctrines of jaundice may be discussed.

I. The notion of a hæmatogenous jaundice is certainly to be found in Aretæus. He speaks of divers causes of jaundice, not only from the liver, but from the stomach, the spleen, the kidneys, and the colon. But, besides jaundice from the viscera, "the general system is most powerful in producing icterus;" and "if indigestion happen in the blood, the blood assumes the

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but he goes on to speak of icteritia of the brain, kidneys, and spleen; of local icteritia of the limbs, and of red, white, and black icteritia. Red icteritia seems to be erysipelas.

* Sylvius de le Boe, *Praxeos med.* Lib. i. cap. xlvi. *Opera medica*, Amstelodami, 1679, p. 301.

appearance of bile, but is distributed as nourishment to all parts, wherefore bile appears everywhere."[*] Galen likewise discusses the question if jaundice may be seen without disorder of the liver. He says he has seen, without any disease of this organ, a critical effusion of bile on the skin, and also that he had seen a change of blood into bile[†] from some strange corruption such as follows the bites of beasts, and for this he instances a case of jaundice following snake bite. This may be due to some change in the humours wrought by the poison. These ideas do not seem to have taken much root among physicians, for there seems to be no mention[‡] of the theory of hæmatogenous jaundice until Bianchi again distinctly enunciated it.[§] This writer speaks of two kinds of jaundice, one caused by disease of the liver, the other by a solution of the blood, in which the motions do not become white, but are rather more deeply coloured. It is more quickly brought about than the other kind of jaundice, and is seen in fevers and after the bites of vipers. This view is shared by certain obscure writers upon jaundice and bilious diseases.[‖] It was upheld for a time by Reil, who, under the name of polycholia, gave a long description of what is now called hæmatogenous jaundice, with rules for distinguishing it from true jaundice.[*] The opinion was resisted by Cullen, who says that jaundice must be the result of bile, once secreted, being taken up into the blood-vessels;[†] by Donald Monro,[‡] Eller,[§] and Selle;[‖] they all teach that the doctrine of jaundice from absorption is the only trustworthy theory.

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[*] Aretaeus, *op. cit.* p. 326. Leo, likewise, says that jaundice may arise from the conversion of blood into bile from heat of the system. (Quoted by Adams in his translation of Paulus Æginetus, vol. i. p. 585.)

[†] ὁρᾶται δὲ καὶ χωρὶς κρίσεως ἐκχολούμενον ἐνίοτε τὸ αἷμα. Galen, *de loc. aff.* Lib. v. cap. viii. ed. Kühn, Lipsiae, 1824, vol. viii. p. 355.

[‡] I have been unable to find any trace of this doctrine in the writings of Sydenham. One passage (*Obs. med.* iv. 3, § 8, *Opera omnia*, ed. Greenhill, p. 170.) is thought by Eisenmann to have a faint likeness to this teaching. To me it seems merely the explanation of a kind of dysentery by invoking a disease of the blood, the hot and acrid humours of which are thrown upon the gut by the mesenteric arteries. Nor can I find anything in Baillou's chapter on the epidemics of 1575, which would remind the reader of the theory. (*Épidémies et éphémérides*, ed. Yvaren, Paris, 1858, p. 278.)

[§] Bianchi, *Historia Hepatica*, Genevae, 1725, 3tia ed. t. i. pars ii. cap. x. p. 185.

[‖] For the bibliography of bilious fevers, see Eisenmann's *Die Krankheits-Familie Cholosis*, Erlangen, 1836.

No further important support is met with until the time of Saunders, who speaks of the experiments of Fourcroy and Vauquelin.[¶] These observers made a sort of artificial bile by heating together ox blood and water. Saunders then adds: "it would appear probable, that, under certain morbid states of the body, the blood *may* acquire a bilious appearance, independent of absorption or regurgitation from the liver."[**] It is worthy of note that the man, who was the first to prove by experiment the doctrine of jaundice from absorption, should likewise have given the weight of his authority to the theory of a hæmatogenous jaundice.

One of the next notices of a jaundice arising from changes in the blood, without any implication of the liver, may be found in the writings of Breschet. After pointing out the near relation which exists between melanosis and the colouring matter of the blood, he says that he presumes that jaundice is brought about much less by the bile than by the blood,[††] and he attributes the jaundice so common in the new born to changes in the circulation rather than in the liver.[*] Later on Virchow contributed much to the spread of this notion of an *icterus paradoxus*. He made known the likeness between hæmatoidin and bile pigment, both in crystallization and chemical reaction.[†] The identity of these two substances was thought to have been proved by Zenker and Funke,[‡] Valentiner,[§] and later still by Jaffe.[‖] But Städeler[¶] and Holm[**] deny this and give rules by means of which hæmatoidin may be distinguished from bilirubin. Salkowski on the other hand, says that a substance, with many of the characters of hæmatoidin, which he found in the thyroid gland, and which must therefore have its origin in the blood, was insoluble in æther, and soluble in alkalies, which Holm and Städeler assert to be characteristic of bilirubin.[††] Thudichum, however, would affirm that the body which all these observers analysed was neither bilirubin nor hæmatoidin but lutein[‡‡] the hæmolutein of Piccolo and Lieben.[§§] Thudichum further protests against the idea of the bile pigments being derived from hæmatoidin because they contain no iron.[‖‖] There is, however, a hæmatin free from iron

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[*] Reil, *Tractatus de Polycholia*, Halae, 1782, p. 47. He withdrew the opinions expressed in this "*juvenile opus*," as he calls it, a few years later, and says that no bile, nor anything like bile is made, save by the help of the liver. (*Memorabil. Clinic.* fasc. iv. Halae, 1795, p. 48.)

[†] Cullen, *First Lines of the Practice of Physic*, § 1817.

[‡] Donald Monro, *An Account of the Diseases which were most frequent in the British Military Hospitals in Germany*, London, 1764, p. 206.

[§] Eller, *Obs. de cog. et cur. morb.* Venetiis, 1767, Sect. ix. p. 177.

[‖] Selle, *De curand. hom. morb.* Berolini, 1798, ed. Sprengel, p. 184.

[¶] Fourcroy and Vauquelin, *Annales de Chemie*, 1790, t. vi. p. 181.

[**] Saunders, *A Treatise on the Structure, Economy, and Diseases of the Liver*, London, 1803, 3rd edition, p. 105, note.

[††] Breschet, *Considérations sur une altération organique appelée dégénérescence noire, etc.* Paris, 1821, p. 21. Andral (*Clinique méd.* Paris, 1839, t. ii. p. 287.)

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would seem, with Breschet, to favour the notion that the colour in the newly born, or in yellow fever, is due to changes in the circulation or to a sort of general ecchymosis. The same thought is before expressed. (t. i. p. 601.)

[*] In the old Chinese system of physiology, the reverse was believed; the liver was the source of all the pigments in the body.

[†] Virchow, *Arch. f. path. Anat.* Bd. i. 1847, p. 370. See also *Ges. Abh.* Hamm, 1862, p. 849.

[‡] Funke, *Lehrb. d. Phys.* Leipzig, 1860, Bd. i. p. 246.

[§] Valentiner, quoted by Steiner, *Arch. f. Anat. u. Phys.* 1873, p. 163.

[‖] Jaffe, *Arch. f. path. Anat.* 1862, Bd. xxiii. p. 192. He obtained bilirubin from an old hæmorrhage into the brain.

[¶] Städeler, *Annal. d. Chemie und Pharm.* 1864, Bd. cxxxii. p. 343.

[**] Holm, *Journal f. prakt. Chemie*, 1867, Bd. c. p. 142.

[††] Salkowski, *Med.-Chem. Untersuch.* Hrsg. von Hoppe-Seyler, 1868, Heft. iii. p. 436. Hoppe-Seyler found bilirubin in a cyst of the breast. (*Arch. f. path. Anat.* 1862, Bd. xxiv. p. 10.)

[‡‡] Thudichum, *Proc. of the Royal Society of London*, 1869, Vol. xvii. p. 255.

[§§] Piccolo and Lieben, *Giornale di scienze naturali ed economiche*, Palermo, 1866, Vol. ii. p. 258.

[‖‖] Thudichum, *Zeitschrift f. rat. Med.* Bericht f. 1868, p. 223.

which is asserted to be polymeric with bilirubin; yet it seems strange that hæmoglobin should so readily part with its iron. Dr. Young found in some careful experiments under Prof. Gamgee's direction that the ash of the bile was rich in iron,[*] and this fact is also worthy of being kept in mind.[†]

Preyer seems decidedly of opinion that hæmatoidin and bilirubin are not the same bodies. He finds that the spectra of the two are altogether different; the colouring power of hæmatoidin is also much weaker than that of bilirubin.[‡] It certainly does seem that no satisfactory elementary analysis of hæmatoidin has yet been made; in Robin's case it is doubtful if he had to do with hæmatoidin at all. With this exception, hæmatoïdin has been examined in but very minute quantities, only to be recognised with the microscope. If the spectra be so entirely different, it will be hard hereafter to maintain the identity of the two bodies, even if the elementary analysis prove to be very similar. Mr. Sorby, however, seems to think that the spectra of bile from snails and of hæmatin are closely akin.[§] It will be necessary, however, to extend this observation to vertebrates, before any result valuable to the physician can be obtained. Maly also found that the crystals of bilirubin showed under the microscope a convex appearance, like that of the section of a biconvex lens.[‖] The crystals of hæmatoidin have always a rhomboidal appearance.

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[*] P. A. Young, *Journal of Anatomy and Physiology*, Vol. v. 1871, p. 158. Robin (*Comptes rendus*, 1855, t. xli. p. 506) found iron in the ash of the red matter found in echinococci cysts in the liver; about ·0002 *per cent.* Robin calls this red matter hæmatoidin, but I venture to express a doubt as to the propriety of so naming it. The source is highly suspicious, and it is known how very often hydatid cysts communicate with the gall ducts. The percentage analysis agrees tolerably closely with that of bilirubin.

[†] See also the discussion of the relation between bilirubin and hæmatoidin at p. 32 of this work.

[‡] W. Preyer, *Die Blutkrystalle*, Jena, 1871, p. 187.

[§] Sorby, *Quarterly Journal of Microscopical Science*, 1876, Vol. xvi. p. 78.

[‖] Maly, *Sitzungsberichte der math.-naturw. Classe d. kaiserlichen Akademie*, Wien, 1868, Bd. lvii. Abth. ii. p. 97.

The notion of the identity of bilirubin and hæmatoidin being once set up in the minds of physiological chemists, it seemed no strange statement that the bile pigments should appear in the urine when any large number of the blood corpuscles were dissolved. This indeed is what Frerichs found after the injection of the bile acids into the blood, a fact explained by him in altogether another way.[*] Kühne, likewise upheld Frerichs' belief, and added a new fact, that the bile pigments appear in the urine after the injection of hæmoglobin into the circulation.[†] M. Herrmann also found these after the injection of large quantities of water into the veins;[‡] Nothnagel, after the injection of æther and chloroform;[§] Munk and Leyden, after the injection of phosphoric acid:[‖] all these bodies having the power of dissolving the red blood-corpuscles and thus setting the hæmoglobin free in the blood-vessels.

The theory of hæmatogenous jaundice seemed thus to receive great support from experiment.

But it was assumed with too great haste that if the colouring matter of the bile were present in the urine, that jaundice was thus of necessity at hand. It is indeed true that the urine is often the first to give notice of a coming attack of jaundice, even before the conjunctiva; but it is well to point out with Virchow[¶]

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[*] Frerichs, *Klinik d. Leberkrankheiten*, Braunschweig, 1858, Bd. i. p. 405. See also *Arch. f. Anat. u. Phys.* 1856, p. 59, note.

[†] Kühne, *Arch. f. path. Anat.* 1858, Bd. xiv. p. 337. See also *Lehrb. d. phys. Chemie*, Leipzig, 1866, p. 89.

[‡] M. Herrmann, *De effectu sanguinis diluti in secretionem urinæ*, Diss. Inaug. Berolin. 1859, p. 23.

[§] Nothnagel, *Berliner klin. Wochenschr.* 1866, p. 31.

[‖] Munk and Leyden, *Die acute Phosphorvergiftung*, Berlin, 1865, p. 129.

[¶] Virchow, *Arch. f. path. Anat.* 1865, Bd. xxxii. p. 120. Poncet has attempted to cause jaundice by the injection of blood under the skin of animals; he found a high-coloured urine was passed, but strange to say, no chemical tests were used. (*de l'ictère hématique traumatique*, Thèse de Paris, 1874, p. 61.)

that in none of these experiments has a real jaundice been brought about. There has never been a yellow staining of the tissues, but only a reaction of bile pigment in the urine; and between these two states there is a deep and wide division. No artificial jaundice has been as yet caused by injecting any quantity of bile into the blood,[*] though it would seem possible that jaundice might follow, if substances which destroy the blood-corpuscles were allowed slowly to act upon the œconomy.

The likelihood of this last observation of Virchow's to be true has of late years somewhat decreased. The foregoing experiments upon which so much stress has been laid have been repeated, and in general, no bile pigment has been detected in the urine after the injection of substances which dissolve the blood-corpuscles. Naunyn was the first to repeat these observations[†] and he could not succeed in obtaining a reaction peculiar to the bile pigment after the injection of hæmoglobin into the circulation or under the skin. In both cases the urine might contain blood colouring matter, but no bile pigment. J. Steiner, likewise, repeated M. Herrmann's observations, and found that no bile pigment was present in the urine after the injection of large quantities of water.[‡] I myself have been unable to detect the presence of bile pigment in the urine after the injection into the circulation of the bile acids, notwithstanding the statements to the contrary of Frerichs and Kühne. Furthermore, Naunyn, after the injection of æther under the skin found well-marked signs of the presence of hæmoglobin in the urine in all cases; but in only one out of four could a certain opinion be given as to the presence of bile pigment.*

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[*] Dr. George Harley indeed states that he has succeeded in making a dog jaundiced by injecting the bile of other dogs under the skin. He failed, however, in two other experiments. (*Jaundice: its pathology and treatment*, London, 1863, p. 96.)

[†] Naunyn, *Arch. f. Anat. and Phys.* 1868, p. 410.

Nasse (*Sitzungsberichte d. Marburg. Gesellschaft*, 1875, No. 2. quoted in Hayem's *Revue des Sciences méd.* 1876, t. vii. p. 530) found that the urine gave no reaction with nitric acid after the injection of large quantities of blood into the stomach of dogs; but (Hofmann and Schwalbe's *Jahresb. d. Anat. u. Phys.* f. 1874, iii. Abth. p. 182.) the same observer is reported to have found that after injecting a great quantity of dissolved corpuscles into the stomach of one dog, the urine shows traces of bile pigment on the second and third day, not the first.

[‡] J. Steiner, *ibid.* 1873, p. 160.

This great difference between observers so trustworthy may, I think, best be explained by the fact that Frerichs, Kuehne and Herrmann seemed to have used for their experiments dogs, in whose urine a substance which gives all the reactions of bile pigment is an almost constant constituent.† Naunyn, Steiner and myself have used rabbits exclusively for experiment, and in the urine of these animals, unless fasting, bile pigment is not often seen. These later experiments would therefore seem more trustworthy than those of Kühne and Frerichs, and I do not think that their value has been destroyed by Tarchanoff's recent observations, for although after the injection of hæmoglobin into the circulation bile pigment was seen in the urine, yet the experiments themselves are not such as to command confidence. In the first place, dogs were used, in some cases even without testing the urine beforehand for bile pigment; and further it was not expressly stated that the animal was not fasting, and most of the experiments lasted over six hours, at the end of which the bile pigment was found.‡ Even this observer found no bile pigment after a six-hours narcosis from chloroform.

Although Breschet was the first to found the doctrine of a hæmatogenous jaundice, supported by Andral, and more lately by less-known names, yet the theory seems to have made little progress in France; and in England the doctrine is but little received, the other view, that of jaundice from suppression, finding greater favour. It is chiefly invoked to explain the phænomena of *icterus gravis*. Under this head may be placed acute yellow atrophy of the liver, the jaundice seen in poisoning from phosphorus, in pyæmia, and other acute diseases. In this way Leyden has laboured to explain the yellowness of the skin sometimes seen in chlorosis, pyæmia, heart disease, or after anæsthesia from chloroform. In these cases the yellowness of the skin is out of all proportion greater than the bilious appearance of the urine. In jaundice from obstruction, the reverse is seen. There is likewise no evidence of the presence of bile acids in the urine in these cases. Further, there is often proof, in the cases of *icterus gravis*, of the circulation of some poison in the blood, able to destroy the red corpuscles, as in poisoning by phosphorus, yellow fever, and the like. The varieties of *icterus gravis* resemble each other in having a tendency to stupor or delirium. In the fatal cases, no impediment can be found, after death, to the flow of bile into the duodenum, the liver itself being free from a jaundiced tint and the fæces containing bile. A far advanced fatty degeneration of all the glandular and muscular organs is likewise found.*

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* Naunyn, *op. cit.* p. 438.

† But this does not explain the matter throughout: Nothnagel used rabbits in all his experiments with æther and chloroform (*Berlin. klin. Wochenschr.* 1866 p. 31) and Kühne (*Lehrb. der phys. Chemie*, p. 89) expressly says that rabbits must be used in the hæmoglobin-injection experiment on account of the constant presence of the bile pigment reaction in the urine of dogs.

‡ Tarchanoff, *Arch. f. d. ges. Phys.* 1874, Bd. ix. p. 53.

I should long hesitate in forming any opinions from the statement that the urine is often less jaundiced than the skin, or that the liver after death shows no jaundiced appearance. Virchow, for instance, formerly thought that a jaundice of the liver preceded a jaundice of the whole body,† but later saw reasons to withdraw this opinion,* and this admission is of the greater importance, since Virchow was undoubtedly the founder in modern times of the doctrine of hæmatogenous jaundice. Nor can I attach much weight to the statement, that in cases of slight jaundice, the urine is much less jaundiced than the skin. I have sometimes found in examining cases of slight jaundice after death, that the serous effusions from the chest and belly gave an intense reaction with nitric acid, while the urine gave but slight indications of the presence of bile pigment with the same reagent. The serous effusions and the urine may, I should think, be looked upon as at least equal in importance for indicating the amount of bile pigment contained in the blood. The cases which I mention have been chiefly those of heart disease.

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* Leyden, *Beiträge zur Pathologie des Icterus*, Berlin, 1866, p. 6.

† Virchow, *Arch. f. path. Anat.* 1847, Bd. i. p. 380.

A point of which much importance has been made by Leyden, is the absence of the bile acids in the urine, in some cases of jaundice. Naunyn's observations have, however, destroyed all value which may be attached to this opinion, for he has shown that the bile acids may be found in every urine, even in that of perfect health.† They appear to be absent in no cases of jaundice, except perhaps at the end of cases of long continued obstruction to the bile ducts, as Golowin has pointed out.‡

It is indeed only from the fatal cases that any safe conclusions can be drawn. The fatal cases of which Leyden speaks all belong to the class of *icterus gravis*. Poisoning by phosphorus would, I think, be accepted as a type of this class. The stools are sometimes coloured, sometimes free from colour. Yet Oskar

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* Virchow, *Arch f. path. Anat.* 1865,Bd. xxxii. p. 121.

† Naunyn, *Arch. f. Anat. und Phys.* 1868, p. 430.

‡ Golowin, *Arch. f. path. Anat.* 1871, Bd. liii. p. 433.

Wyss* and Ebstein† found in the livers of dogs and men poisoned by phosphorus, that the finer ducts within the liver were plugged with a colourless mucus which hindered the descent of the bile; a plain cause of jaundice. While this explanation of the jaundice remains available, it seems to me imprudent, to say the least, to search for other and less likely causes elsewhere.

The presence of deeply coloured stools cannot always be received as proof of the freedom of the hepatic ducts. Indeed, in jaundice, the more deeply coloured the stools, the greater suspicion should be aroused. It is well known that many substances given by the mouth make the stools dark, as charcoal, iron, or bismuth. What is more important in the present discussion is that blood passed into the alimentary canal causes the stools to have a very high colour; now in *icterus gravis* hæmorrhages are very common and especially abundant in the stomach and intestines. It is therefore not surprising to find that in many cases the stools are reported to be dark. In a case of my own, I found that the fæces in the large intestine were clay-coloured; in the small intestine they were dark, almost black. In jaundice I look upon the absence of colour in the stools as tolerable proof that some of the bile ducts are obstructed; but I cannot accept the presence of colour in the stools as proof that the ducts are free.

As Leyden has been the champion of hæmatogenous jaundice in Germany, so Gubler has been in France. In 1857 he published a case of poisoning by lead, complicated with jaundice. The urine was very high coloured, and to the eye alone presented precisely the appearance of ordinary jaundiced urine. It gave, however, no distinct reaction with Gmelin's test, and Gubler from this single circumstance calls the case one of *ictère hémophéique.*[*] There is, strange to say, no account of the state of the stools; so the case proves nothing. The same strange disregard of an important appearance runs through the table of elaborate distinctions given by Michel, a pupil of Gubler, the theory of which may be at any moment upset by an inspection of the *fæces alvinæ.*[†] The cause of this kind of jaundice is, according to Gubler, the inability of the liver to separate from the blood the colouring materials for the formation of bile, when from some cause or other there is too rapid destruction of the red globules. This blood pigment, free in the blood, Gubler calls hæmophæin.[‡] This is evidently a revival of the old doctrine of suppression, allying itself to the newer theory of hæmatogenous jaundice. It is used to explain the jaundice in febrile disorders and of the new born, as well as that which follows catarrh of the stomach.[§] Gerhardt endorses many of Gubler's opinions. He calls the pigment in the urine urobilin, but solely because the extract of the urine with chloroform gives a fluorescence into green-yellow when treated with choride of zinc and ammonia.[*]

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* Oskar Wyss, *Arch. d. Heilkunde*, 1867, p. 469.

† Ebstein, *ibid.* p. 506; and 1869, p. 379. I have myself verified the statement that the smaller ducts may hold bile, the larger a colourless fluid. (*Trans. of the Path. Soc.* 1874, Vol. xxv. p. 161.)

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[*] Gubler, *Union méd.* 1857, p. 503. Hæmaphæin is the name used by Franz Simon for the natural colouring matter of the urine, and which he believed to be derived from the red blood corpuscles. (*Animal Chemistry*, Sydenham Society's Translation, 1845, Vol. i. p. 159, and Vol. ii. p. 119.)

[†] Evariste Michel, *de l'ictère hémaphéique*, Thèse de Paris, 1868, pp. 14, 16, and 18. In the cases there is also no word about the stools. Dreyfus-Brisac, another disciple of Gubler's, does indeed at the end of his table of distinctions mention that the stools in hæmaphæic jaundice are: *très-variables, parfois un peu décolorées, le plus souvent très-colorés;* (*De l'ictère hémaphéique*, Paris, 1878, p. 40) but in his cases he seems to have paid very little attention to the stools at the height of the disease, and only when the jaundice is fading does he remark how deeply coloured they are; a state which may readily be explained without resorting to Gubler's hypothesis.

[‡] Rendu gives a just account of Gubler's views in an excellent article in the *Dictionnaire encyclopédique des Sciences méd.* Foie (pathologie) 4e Série t. ii. p. 680.

[§] Laborde praises Gubler highly: "M. Gubler, il faut bien le dire, l'a faite complétement sienne par la précision apportée dans l'analyse des faits, l'exacte appréciation des phénomènes, et les développements qu'il n'a cessé de lui donner, en prenant pour base les faits cliniques." (*Physiologie pathologique de l'ictère*, Thèse pour l'agrégation, Paris, 1869, p. 69.)

Poncet has also published a thesis in which he attempts to establish a jaundice from the destruction of the blood corpuscles after great extravasations of blood. This observer is of opinion that hæmatogenous jaundice can no longer be denied. He has seen, after great extravasations of blood in the limbs or trunk, a slight jaundice arise. This jaundice he says is due to the destruction of the red corpuscles, and the increased colour of the urine is due solely to an increase of the urobilin. Nothing here, too, is said of the state of the stools. Poncet only brings forward one case examined after death; and in this, strange to say, no account of the liver seems to be recorded.[†] This writer adds but little to the evidence already given in favour of hæmatogenous jaundice: and a word of warning has been addressed to him by Paul Cazeneuve who could find no increase of the colouring matters of the urine, nor any bile pigments in the urine after the subcutaneous injection into a rabbit of 10 to 20 C. C. of blood, or ·05 to ·1 grm. of hæmatin.[‡]

The following case, which Immermann calls one of hæmatogenous jaundice, is certainly well worthy of attention.

Christian Rupaner, aged 23, born in Baden, was admitted into the Hospital at Basel on January 23. 1873. For eleven days before, he had been suffering from symptoms of a moderately severe attack of typhoid fever. The course of the disease was regular and uncomplicated; it was treated with quinine in large doses, and with baths as often as the temperature rose. On Feb. 21. there was a relapse, treated as the first attack. On Feb. 27. the urine was slightly albuminous and contained pus cells. On March 1st a slight jaundiced tint began about 7 a.m. and at 9. a.m. the tint was deep; liver natural. Continual vomiting of bilious matter and two highly bilious stools in the course of the morning. At the same time the urine was scanty and almost black. It gave no trace of bile pigment, but became almost solid on boiling, and showed Heller's test for blood. Under the microscope no red corpuscles, only pus corpuscles were seen. On March 2. the jaundice was the same; vomiting, four bilious stools. The urine albuminous as the day before, no red blood corpuscles in sediment but some well preserved pus corpuscles. With the spectroscope, oxyhæmoglobin and hæmatin were in the urine; no bile pigment. On March 3. the jaundice of skin and conjunctiva much decreased. Vomiting continued with diarrhœa and bilious stools. The urine yellow brown, highly albuminous, containing neither blood colouring matter nor bile pigment. On March 4. jaundice gone; vomiting and albuminuria continuing till death. On March 9. the patient died comatose, no jaundice and no blood in water being again seen. After death the kidneys were found in a state of acute parenchymatous degeneration. In the small intestine bilious fluid; on pressing the gall-bladder, a hyaline plug escaped from the gall ducts into the duodenum. The lower part of small intestine showed freshly-healed typhoid changes. In the liver there was some over growth of the connective tissue.*

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[*] Gerhardt, *Correspondenz-Blätter des allgem. aerzt. Vereines von Thüringen*, 1878, Jahrg. vii. No. ii. Nov. 20.

[†] A. Poncet, *de l'ictère hématique traumatique*, Thèse de Paris, 1874, p. 40.

[‡] P. Cazeneuve, *Gaz. méd. de Paris*, 1877, p. 271.

The reader should note, in forming a judgement on this case, that the liver and the ducts were not free from disease. The liver was in an early stage of cirrhosis, and the extremity of the gall duct held a plug of mucus. It is true that no bile pigment was found in the urine, but it is possible that the large amount of albumen present in the urine may have had the effect of masking the ordinary Gmelin's reaction. Bile acids were not looked for.

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* Immermann, *Deutsches Arch. f. klin. Med.* 1874, Bd. xii. p. 502. The case is fully given.

The grounds on which the theory of hæmatogenous jaundice have been set up are, to my mind, altogether insufficient. It cannot be said that the origin of the colouring matter of the bile from that of the blood is proved; indeed of late the course of discovery has been rather against their identity than in favour of it. And until it have been shown that bile pigment has its source in the blood-corpuscles, it will be the duty of the practical physician to reject the theory of hæmatogenous jaundice.

II. The second kind of jaundice is that of jaundice by suppression. The great doctors of the seventeenth, and early part of the eighteenth, centuries, taught that the secretions existed ready formed in the blood, and that the glands merely acted as filters to strain the excretions from the circulating mass. Glisson speaks thus of the liver.[*] The doctrine of jaundice from suppression of the secretion was a natural outcome of this physiology. It is therefore to be found in the writings of Morgagni, who distinctly attributes the jaundice in case of obstruction not to the absorption of bile already secreted; but, because the bile ducts are already filled by secretion, the bile cannot enter them, and thus accumulates in the blood.[†] Van Swieten, likewise, speaks of two kinds of jaundice; one from an impediment to the free exit of the bile from the bile ducts; the other, from a hindered secretion.[‡] Towards the end of the eighteenth century, this view of jaundice began to lose ground, even before the experiments of Saunders. It continued, however, to be taught and acted on by many noted physicians.

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[*] Glisson, *Anat. Hepat.* Cap. xxxviii. *et seqq*. Amstelædami, 1659.

[†] Morgagni, *De sedibus, etc.* Ep. xxxvii. Art. 9.

[‡] Van Swieten, *Comment.* § 950, Lugd. Bat. 1755, t. iii. p. 127.

Andral,[*] Sir Thomas Watson,[†] Bamberger,[‡] Griesinger[§] and Trousseau[‖] have all supported the doctrine of jaundice by suppression. Dr. Budd[¶] considers this kind of jaundice to be by far the most common. He believes, however, that the colouring matters only are made in the blood, while the bile acids are formed in the liver itself; a view which is supported by Skoda[**] and Dr. George Harley.[††] But about the date of the publication of the first edition of Dr. Budd's book, the doctrine of the formation of the bile in the blood fell into discredit with physiologists, and in our own day, with the exception of one or two supporters, is universally disbelieved. With this, as a matter of course, the notion of a jaundice from suppression of secretion fell too.

The turn of the tide of medical opinion may be noted when Liebermeister, fifteen years ago, pointed out that he did not think the doctrine of the non-existance of the elements of the bile in the blood so surely proved as others then thought. One of his reasons is that jaundice sometimes breaks out after the liver cells have completely disappeared.[§§] There is no proof, however, that this statement of Liebermeister's is correct. No doubt he has shown that in a large number of cases, hitherto unsuspected, the liver cells are destroyed; in many cases of pyæmia, puerperal and typhoid fever: but I do not think he has proved that the jaundice has ever arisen after the complete destruction of the secreting tissue of the liver. Some writers have thought that acute yellow atrophy affords the best proof that the bile is made in the liver, because towards the end of the disease, as the liver cells are destroyed, but little pigment is found in the urine, and no bile acids.*

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[*] Andral, *Clinique méd.* Paris, 1839, t. ii. p. 286.

[†] Thomas Watson, *Lectures on the Principles and Practice of Physic*, Lecture lxxv. London, 1857, Fourth ed. Vol. ii. p. 602. He says that Darwin was the first to introduce into this country the doctrine since supported by Chevreul and Mayo. Erasmus Darwin (*Zoonomia*, Lond. 1801, Vol. ii. p. 5) speaks of a paralysis or inability of the secretory vessels of the liver, but without bile in the stools or urine, and a skin like the colour of full-grown silkworms. It may well be doubted if he speak of a jaundice.

[‡] Bamberger, *Krankheiten des chylopoëtischen Systems*, Erlangen, 1857, p. 517.

[§] Griesinger, *Infectionskrankheiten*, Erlangen, 1857, p. 78.

[‖] Trousseau, *Clinique méd. de l'Hôtel Dieu*, Paris, 1865. 2e éd. t. iii. p. 274. His opinions expressed elsewhere make it doubtful if he always held this belief.

[¶] George Budd, *On Diseases of the Liver*, London, 1845, p. 373.

[**] Skoda, *Deutsche Klinik*, 1859, p. 286.

[††] George Harley, *Jaundice*, London, 1863, p. 20.

[‡‡] Liebermeister, *Beiträge zur path. Anat. u. Klinik d. Leberkrankheiten*, Tübingen, 1864, p. 241.

Dr. Moxon thinks that the colourless contents of the ducts in cases of long continued obstruction prove that the bile is not formed in the liver, and that all cases of jaundice are caused by suppression of the secretion, not by reabsorption of secreted bile.† His views closely resemble those of Morgagni quoted above, but it cannot be thought that he has brought forward much evidence in favour of his belief.

Jaccoud is inclined to the belief that in long-continued jaundice the liver ceases to secrete bile.‡ To this view there is but little physiological objection; for it is not improbable that a liver severely damaged should cease to secrete bile, and that the jaundice should thereupon decrease. It is very different to the statement that jaundice may be caused by suppression of the functions of the liver.

The theory that the bile was not formed by the liver was thought to have been disproved by Johannes Mueller, Kunde, and Moleschott§. This last observer found that frogs, after their liver had been taken away, lived nearly three weeks, and yet no trace of bile could be found in the blood, muscles, gastric juice, lymph, or urine. The vital processes in these cold-blooded animals are, however, but slow. Leyden tied the common duct of frogs, and after 8 to 14 days found no trace of jaundice in the liver,* so that if no jaundice be caused by ligature of the common duct, it would not be strange that none should arise after the taking out of the liver. If these experiments of Leyden's be trustworthy, a very important support to the view that the liver forms the bile is taken away.

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* Hilton Fagge, *Guy's Hospital Reports*, 1875, p. 174.

† Moxon, *Trans. of the Pathological Society of London*, 1873, Vol. xxiv. p. 133.

‡ Jaccoud, *Leçons de Clinique méd.* (Lariboisière) Paris, 1873, p. 543.

§ See p. 83 of this work.

Another fact thought to favour this last view is that the bile acids and bile pigments cannot be found in the blood, even in the blood of the portal vein. Of this last there is usually so little to be had that there is scarcely enough for a trustworthy analysis. But I believe that no observer in modern times has been able in health with certainty to detect any of the elements of the bile in the blood. Naunyn, however, has found small but appreciable amounts of bile acids in the urine of healthy men:† and it is no uncommon thing to find that the urine of men and dogs shows traces of the presence of bile pigment: and this is especially the case after long fasting, when, that is to say, the liver has not for some time been stimulated to excrete much bile. It may further be alleged that if the elements of the bile be formed in the blood, it would be unlikely that they should be found in the serum. The liver seems, as shown by the experiments quoted just above, to have the power of rapidly secreting into the bile ducts all the bile pigment and bile acids which may be brought into the blood. On the other hand it may be pointed out that Schmulewitsch has succeeded in keeping up a continuous secretion of bile for two or more hours after death by causing the same blood to pass and repass many times through the liver, a phænomenon opposed to the notion that the bile is simply separated by the liver.* Pflüger has, however, repeated Schmulewitsch's experiments in a dead liver with three *per cent.* saline solution, and has found an apparent abundant secretion of bile. He thinks there is no real secretion of bile, but a transudation into the ducts pushing the bile already made before it.† Röhrig has repeated both Schmulewitsch's and Pflüger's experiments, and finds that bile is secreted when blood is passed through the vessels, while none flows out when saline solution is used.‡

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* Leyden, *Beiträge zur Path. des Icterus*, Berlin, 1866, p. 19. He does not, however, expressly say that he examined the blood or urine; nor does he say that he fed the animals, a point of importance in judging of matters allied to the digestion and general powers of life.

† Naunyn, *Arch. f. Anat. u. Phys.* 1868, p. 430.

The presence also of a small quantity of the bile pigments and bile acids in the urine may be explained by supposing that they have been absorbed from the bile passages after secretion. Such was the belief of Dr. Bence Jones,§ who says that the bile begins to pass out of the gall bladdder as soon as it is passed into it. Of this statement it must be admitted, however, that very little direct proof exists.

Some authors, especially Dr. Murchison,‖ have looked upon the fact that in some cases of diseased livers without jaundice, no bile can be found in the bile ducts, as evidence in favour of the view that the bile is formed in the liver. Dr. Hilton Fagge, in a paper lately published,* admits that this would be good evidence, were the liver diseased in all the cases in which the bile ducts were unstained. He then quotes Dr. Moxon's authority for saying that in only one out of four such cases observed by him, was the liver diseased,† the other three being cases of pyæmia and pneumonia. The liver is so commonly diseased in these two morbid states, and as commonly overlooked, that it would be desirable to have further evidence as to the state of the liver, before deciding that the liver is not always diseased when the ducts are free from colour.

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* Schmulewitsch, *Arbeiten aus der phys. Anstalt zu Leipzig*, iii. Jahrg. 1868, p. 113.

† Pflüger, *Arch. f. d. ges. Phys.* 1871, Bd. iv. p. 54.

‡ Röhrig, Stricker's *Med. Jahrbb.* Wien, 1873, p. 267.

§ Bence Jones, *St. George's Hosp. Reports*, 1866, Vol. i. p. 190.

‖ Murchison, *Clinical Lectures on Diseases of the Liver*, London, 1868, p. 305. I think these cases of colourless mucus in the bile passages without jaundice are somewhat rare. Upon Haspel's cases (*Maladies de l'Algérie*, Paris, 1850, t. i. p. 262) I think much weight can scarcely be laid. He is speaking of abscess of the liver in which there was almost complete destruction of the organ. He adds that the bile was no longer secreted, and the bladder contained only a little white mucus. He does not speak of the state of the other bile passages. See also cases reported by Andral, (*Clinique méd.* Paris, 1839, t. ii. p. 275.) Frerichs, (*op. cit.* Bd. i. pp. 86 and 322.) and Wertheimber. (*Fragmente zur Lehre vom Icterus*, München, 1854, p. 3.)

Gubler, according to his interpreter Michel, appears to have formulated a theory of jaundice which unites the idea of suppression of the functions of the liver with a change in the blood. Michel, giving inedited tables of Gubler's,‡ says: "The exciting cause of hæmaphæic jaundice is an inability, absolute or relative, of the liver to separate from the blood the materials destined for the formation of bile, and especially the colouring matter derived from the destruction of the globules and to which Gubler gives in general the name of hæmaphæin. The proportion of this colouring matter, the source of that of the bile, being normal, the liver sometimes falls into a state of torpor, or the liver continuing its functions, the destruction of the globules becomes sometimes excessively rapid, and brings into the circulation waste material which the liver cannot transform.

"The remote causes of this kind of jaundice would thus be those which paralyse the secreting functions of the liver, either by preventing the bringing to this organ of materials upon which it acts, or by striking the parenchyma with inertia. Thus hæmaphæic jaundice is seen most commonly in acute phlegmasiæ with rapid destruction of the red corpuscles: such as pneumonia, acute rheumatism, in poisonings, such as yellow fever, pyæmia, agues: in the *embarras gastrique* and the jaundice of the new born."

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* Hilton Fagge, *Guy's Hospital Reports*, 1875, p. 172.

† Moxon, *Trans. of the Path. Soc. of London*, 1869, Vol. xx. p. 220.

‡ Apparently derived from αἷμα and φαιός, dusky dun, grey, Latin *fuscus*. (See Simon, *Animal Chemistry*, 1845, Sydenham Society Trans. Vol. i. p. 42.) *Ictère hémophéique* appears as the title of a case by Gubler in the *Union méd.* for 1857, p. 503.

Gubler, according to the same author, looks upon the following appearances as diagnostic of this variety of jaundice, as distinguished from that caused by a hindrance to the flow of bile: The tint of the patient slight, sometimes deep, but in every case a little dull; no itching or exanthemata; the serum of the blood and closed cavities, when acted on by nitric acid, shows a brown colour; the slow pulse is but a temporary symptom, seen in convalescence; the urine is an amber red or like strong tea; it stains linen reddish; which, when dried, is of the colour of salmon or weak rhatany decoction; of feeble dyeing power; nitric acid gives a colour, more or less deep, of brown red, and gives no precipitate of biliary resin, ordinarily taken for albumen.*

The views of Gubler seemed to have been based on a case of lead colic, in which jaundice was a well-marked symptom.† It is therefore the more noteworthy that, in this case, upon which so much depends, no record should appear of the state of the stools. The views of this observer seem to me so crude and ill-digested that I do not think it will be worth while further to discuss them.

It will be seen that very little evidence as to the place in which the bile pigments and bile acids are formed is in existence; but that what little evidence there is may be cited in favour of the view that these bodies are formed in the liver. This being the case, physicians have no right to found a theory of jaundice which demands a contrary physiological theory, for theories in medicine must be framed in consonance with those views for which there is the greater evidence.

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* Michel, *De l'ictère hémaphéique*, Thèse de Paris, 1868, pp. 14, 16, and 18. Cf. Laborde, *Physiologie pathologique de l'ictère*, Thése de Paris, 1869, p. 91.

† Gubler, *Union méd.* 1857, p. 503.

III. The third theory of jaundice is that which attributes this symptom to the absorption into the blood of bile already excreted by the liver. It is beyond all doubt the best founded of the theories of jaundice; and the one to which the morbid anatomist, as well as the experimental pathologist, will be the most inclined; as in the great majority of cases of jaundice which are examined after death, some obstruction to the flow of bile into the duodenum is undoubtedly found.

It has been seen that, very early in the history of medicine, obstruction to the bile ducts was looked upon as a cause of jaundice. No distinction, however, was made between the effects of an obstruction to the hepatic and the cystic duct; and Morgagni had to teach that the cystic duct could be obstructed without jaundice being caused. This writer did not, however, look upon the absorption of secreted bile as the cause of jaundice. He thought that the bile was unable to pass from the liver into the ducts, these being already over-filled, and that jaundice was caused by suppression of secretion. This doctrine, however, was overthrown at the end of the last century by the experiments of Saunders. He threw a ligature around the bile duct of a dog; it was killed in two hours after. A bilious coloured fluid was seen in the absorbents around the parts and near the thoracic duct. The serum of the blood taken from the jugular vein gave a yellow tinge to white paper dipped in it; much less, however, than the serum from the hepatic veins, the deeper colour of which was well-marked.[*] From these two experiments Saunders thought that it was proved that the absorbents as well as the hepatic veins are concerned in the bringing forth of jaundice.[†]

For nearly a hundred years this theory of jaundice from absorption has held its own, and been assented to by every physician and pathologist who has written on the subject. Among the theories of jaundice it is the only one grounded upon observation and experiment, and the only one to which universal assent may be demanded.

The kinds of jaundice from absorption have been described:

i. Jaundice from obstruction of the ducts.

ii. Jaundice from absorption of the bile when the pressure in the blood-vessels of the liver is decreased.

iii. Jaundice from incomplete destruction of the bile absorbed into the blood.

i. It is well known from the experiments of Heidenhain that the pressure under which bile is excreted is extremely small.[‡] In guinea pigs, the bile ceases to flow down the ducts when opposed by a column of water only 20 centimeters high, and prefers to pass

[*] Saunders, *A Treatise on the Structure, Economy, and Diseases of the Liver*, London, 1803, 3rd ed. p. 111.

[†] Lately repeating Saunders' experiment, I was unable to arrive at the same results as he did. (*St. Bartholomew's Hospital Reports*, 1873, vol. ix. p. 176.) Frerichs likewise (*op. cit.* Bd. i. p. 99) says he has been unable to discover any bile pigments in the blood, serum, or lymphatics, twenty-four hours after the ducts have been tied. Saunders seems to have tied the hepatic duct; in my own experiment the common duct was tied. I have no doubt of the general accuracy of Saunders' conclusions.

[‡] Friedländer and Barisch, *Arch. f. Anat. Phys.* &c. 1860, p. 666. Kowalewsky (Pflüger's *Arch. f. d. ges. Phys.* 1874. Bd. viii. p. 597.) found the pressure of the bile in woorarised cats somewhat higher, from 12 to 20 mm. of mercury; and varying, in direct ratio, with the arterial blood pressure. There is another very instructive experiment of Heidenhain. (*Stud. des phys. Instituts zu Breslau*, 1868. Heft. iv. p. 232.) He allowed a solution of indigo-carmine to flow under small pressure into the bile ducts: the mucous membranes, especially the conjunctiva, of the animal soon became blue; the urine likewise.

into the circulation. It will be seen from this fact how little obstruction to the passage of the bile into the duodenum is needed to cause the bile to flow back into the blood. Nor is it necessary that the obstruction should be complete, but merely that the bore of the duct should be narrowed enough to cause the bile to pass with some trouble into the bowel. It would almost seem that the bile passes as readily into the circulation as into the duodenum. Thus jaundice may easily be caused by a hyperæmic or catarrhal swelling of the part of the common duct which passes through the walls of the duodenum, and yet after death all trace of swelling will have disappeared, and the duct will be fully patent. The only proof of the existence of an obstruction is the finding of the part of the duct below the obstruction uncoloured by bile. Even this evidence may be wanting if the examination have not been made with care enough; for the least pressure on the gall-bladder will send the bile down the common duct into the bowel, staining the duct of a bilious colour. More obvious causes, such as the presence of a calculus in the duct, or the pressure of a tumour from the outside, need not here be spoken of.

ii. The second kind of jaundice from absorption is that which takes place when the pressure of the blood in the vessels of the liver is decreased. This is Frerichs' theory of jaundice. He says that, of the two products of the liver cells, bile and sugar, one passes into the hepatic vein, the other into the capillary bile ducts. The flow of fluid towards the blood can only take place by diffusion; towards the bile ducts, by filtration. How the two are separated is unknown. It must be assumed either that the rapidity of the diffusion into the blood of the elements of the bile is greater than that of sugar; or that the sugar has some attraction to some element of the blood which is wanting to the bile. This last hypothesis is improbable, for no constituent of the blood is known to possess an attraction for sugar. On the first hypothesis, the separation of the two substances would be incomplete; some of the bile passing into the blood, and some of the sugar into the bile; which, indeed, is really the case.[*] If, therefore, the pressure of the blood upon the sides of the vessels in the liver be decreased, the bile will pass in that direction where there is least resistance, that is, into the circulation, and thus jaundice will arise.[†] Heidenhain has given experimental evidence of the truth of this hypothesis. He found that on decreasing the pressure of the blood in the vessels of the liver, the bile already formed began to pass into the circulation.[‡] Frerichs would in this way explain the jaundice seen in cases of plugging of the portal vein, in cases of pigment liver, where a part of the capillaries is filled by masses of pigment, the jaundice seen in the new-born, and after bleeding from the roots of the portal vein, as in yellow fever. This theory of jaundice must undoubtedly be allowed a place equal in probability to that of jaundice from obstruction. It may prove serviceable hereafter in explaining the jaundice which so suddenly arises after mental emotions, the bites of serpents, and after great general bleeding.[§]

iii. The last theory of jaundice which remains to be discussed, is that which attributes the symptom to incomplete destruction of the bile absorbed into the blood.

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[*] C. Ludwig, *Lehrb. d. Phys. des Menschen*, Leipzig and Heidelberg, 1856. Bd. ii. p. 232.

[†] Frerichs, *op. cit.* Bd. i. p. 89.

[‡] Hedenhain, *Studien des phys. Instituts zu Breslau*, Leipzig, 1868. Heft. iv. p. 238.

[§] In this way I should be inclined to explain the jaundice seen in the two first cases recorded by Mr. William Smith. (*Brit. Med. Journal*, 1869. Vol. ii. p. 5.) The jaundice appeared on the first and fifth days after great general bleeding. The stools were light coloured. In the two last cases I feel scarcely disposed to connect the bleeding with the jaundice.

In health the greater part of the bile pigment and bile acids poured into the duodenum is taken up again during the passage of the food through the small intestine. The bile, therefore, finds its way into the radicles of the portal vein, and undergoes a change of some kind, probably oxydation, after which it is thrown out of the system. When this metamorphosis of the bile in the blood is checked or brought to a standstill, jaundice comes on.

This theory may be found in the writings of Daniel Sennert, who speaks of an excess of bile secreted by the liver, which cannot be excreted by the accustomed passages. In this disease, he says, not only is the urine coloured saffron, but the fæces are also highly coloured. Fever is present and the hands and feet are hot.[*] Distinct traces of the same doctrine may be found in the writings of Cullen, who regards it with disfavour;[†] and in those of Portal[‡] and Gardien[§] who approve. Frerichs had, no doubt, some such theory in mind when he speaks of a jaundice, quite independent of the liver, caused by decreased decomposition and change of the bile in the blood. He rests, however, too much upon observations which are now known to be incorrect, those of the change of the bile acids into bile pigment.[||] The late Dr. Murchison may be looked upon as one of the most prominent modern defenders of this theory, and the following account of it is taken from his work.[¶]

The greater part of the bile after having been poured into the intestine is taken up by the radicles of the portal vein, and thus passes into the general mass of the blood. In health, the bile suffers a decomposition, probably an oxydation, and is cast out of the system by the lungs or kidneys. But in some diseased states, this change does not take place; and the bile circulates with the blood, causing a jaundice. The diseased states which hinder these changes of the bile from taking place are: i. The action of certain poisons on the œconomy; they are chiefly those poisons which cause an acute parenchymatous degeneration of the glands and muscles. ii. Nervous influences, as fright. iii. Bad hygienic conditions: and iv. a very great increase in the secretion of bile, so that more is poured out into the gut than can be taken up and changed in the blood into colourless material: a jaundice therefore arises from the circulation of bile pigments in the blood.

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[*] Dan. Sennert, *Epitome universam doctrinam summa fide complectens*, edid. Bonetius, Col. Allob. 1655. p. 681.

[†] Cullen, *First Lines of the Practice of Physic*, § 1817.

[‡] Portal, *Histoire de l'Académie royale des Sciences*, 1777, *Mémoires*, p. 604.

[§] Gardien, *Traité complet d'accouchements*, Paris, 1816, t. iv. p. 95.

[||] Frerichs, *op. cit.* Bd. i. p. 94.

[¶] Murchison, *Clinical Lectures on Diseases of the Liver*, Lond. 1868. p. 375.

This theory rests for support chiefly on the observations of Bidder and Schmidt who found only slight traces of bile in the fæces of dogs.[*] But Hoppe-Seyler ten years after, found abundance of cholalic acid and undecomposed biliary acids in the fæces of dogs. He looks upon cholalic acid as a product of a fermentation or sort of digestion of the bile acids, very like the splitting up of hippuric acid into glycocoll and benzoic acid in decomposing urine.[†]

In the present state of knowledge it cannot be said whether the whole of the bile secreted be at once cast out of the body or not. Schiff and his followers would say that the greater part of the secretion, bile acids and bile pigment, is reabsorbed into the blood, and again excreted by the liver.[‡]

Granting, however, that the liver has this power of again excreting the bile, it is quite unlikely that such absorption of bile should ever become the cause of jaundice. For all the bile absorbed by the vessels is at once carried by the portal system to the liver. The liver, on the showing of Schiff[*], and Tarchanoff,[†] would draw to itself the bile acids and bilirubin in the blood, and forthwith excrete them in the bile. Accepting Schiff's views then, it would therefore seem most likely that if any bile acids and bile pigments were absorbed by the intestine, they would again appear in the bile without entering the general circulation; and without entering the general circulation no jaundice can be brought about.

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[*] Bidder and Schmidt, *Die Verdauungssäfte und die Stoffwechsel*, Mitau and Leipzig, 1852, p. 217.

[†] Hoppe, *Arch. f. path. Anat.* 1862, Bd. xxv. p. 181; 1863, Bd. xxvi. p. 535.

[‡] See p. 147 *et seqq.* for a discussion of this.

The only instance in which this theory, to my mind, can be entertained, is the case of a permanent obstruction of the circulation through the portal vein. This vessel has been artificially obliterated, and traces of the bile acids and bile pigment were found in the urine, traces, however, which soon disappeared.[‡] It is known that in cases of thrombosis of the portal vein jaundice is a common symptom; but it also appears to be a permanent, and not merely a passing phænomenon.

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[*] Schiff, *Arch. f. d. ges. Phys.* 1870, Bd. iii. p. 598; and *Giorn. di Scienze nat. ed econ.* Palermo, 1869, Vol. iv. p. 9.

[†] Tarchanoff, *ibid.* 1874, Bd. ix. p. 332. See also Feltz and Ritter, *Journal de l'Anat. et de la Phys.* 1870, p. 315. The experiments of Huppert (*Arch. d. Heilkunde*, 1864, p. 244) and of E. Bischoff (*Zeitschift f. rat. Med.* 1864, Bd. xxi. p. 125) would seem in some degree to be against Schiff and Heidenhain. Huppert after injecting bile acids into the blood found only a fourth or a third excreted by the liver. What becomes of the rest? The kidneys do not excrete them. According to Bischoff, they are oxydised in the blood. This power of oxydation has, however, a limit; this limit is passed in jaundice, and bile acids appear in the urine.

[‡] Schiff, *op. cit.* p. 609.

CHAPTER XI.

THE SYMPTOMS OF JAUNDICE.

THE first change from health to jaundice is seen in the colour of the conjunctiva. It becomes yellow. This is the symptom commonly first noticed by the friends of the patient, a day or two before the skin has changed its hue. In the lower orders it may often be found that the change of colour in the face is the first to draw attention, the yellowness of the eyes having been passed by. With the better classes, the eyes are commonly the first to be noticed. When the eyes show the first appearance of yellowness, however slight it may be, the urine will also give a good reaction with Gmelin's test, showing the presence of bile pigment. How soon these symptoms set in after the obstruction to the flow of bile is first set up, there are at present no very certain means of judging. It is usually said that they appear after the third day of obstruction;[*] but this conclusion is drawn from observations upon dogs. In these animals the conjunctiva has a brownish appearance, very unlike the pearl white of a human sclerotic, and I look upon this as a hindrance to the early detection of changes of colour. From observations upon men, I should be inclined to put the first appearance of jaundice much earlier after obstruction; perhaps within the first twenty-four or forty-eight hours. In this opinion I am supported by several clinical observers.[†] The serous exudations will sometimes after death give a reaction with Gmelin's test when little or no trace of jaundice exists in the skin.

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[*] Frerichs, *Klinik d. Leberkrankheiten*, Braunschweig, 1858, Bd. i. p. 99. In my own experiments upon cats, the conjunctivæ did not become discoloured for many days after the operation. (*St. Bartholomew's Hosp. Reports*, 1873, Vol. ix. p. 161.)

[†] Siebert, *Diagnostik d. Krankheiten des Unterleibes*, Erlangen, 1855, p. 283. Audigné (*Gaz. méd. de Paris*, 1874, in Virchow and Hirsch's *Jahresb. f.* 1874, Bd. i. p. 349) found that bile pigment could be detected in the urine in three to four hours after ligature of the common duct of a dog. As the urine of dogs so often contains in health a body which gives a reaction precisely similar to that of bile pigment, this observation can be scarcely looked upon as conclusive.

After the conjunctiva, the skin of the face becomes yellow. At first it may be no more than a sallow tinge, hard in some persons to tell from the natural tint of the skin. This is especially the case with persons of dark complexion. Those who are fair show the change earlier. From the face it spreads over the upper part of the trunk and thence over the belly and limbs, the legs being the last to show the yellow tint.

As a rule, the yellow colour of the skin is spread all over the body, no part being more deeply stained than the other. It is, however, not uncommon to see, in cases of slight jaundice, the upper part of the body yellow, while the belly and legs are free from unnatural colour. Frerichs has made the same observation,[*] and Hecker has noticed a case of acute yellow atrophy in which the upper part only of the body was coloured yellow.[†] But in all cases of severe jaundice which have fallen under my observation the whole of the body has been nearly equally jaundiced.

In some old authors,[‡] a jaundice limited to the right half of the body and of the face and hands[§] (*icterus dimidiatus*) has been described. I scarcely feel able altogether to reject these statements when an observation of a like kind has been recorded by so credible a witness as Joseph Frank. He found a lady to have at first jaundice of

[*] Frerichs, *op. cit.* Bd. i. p. 112.

[†] Hecker, *Monatsschrift f. Geburtsk.* 1863, Bd. xxi. p. 212. Cf. van Swieten, *Comment*, § 950, Lugd. Bat. 1755, t. iii. p. 141.

[‡] Behrens, *Ephemerides Nat. Cur.* Noriberg. 1715, Centuria iii. obs. lxiv. p. 145. An old man, seized with right hemiplegia, had jaundice of the same side of the body as the hemiplegia: the right side of nose was yellow, the left natural in colour. Behrens quotes from Ettmüller (*op. med.* Francof. ad Moen. 1697, t. ii. p. 844) a similar case. I have been unable to verify the reference. Morgagni (*De sedibus, etc.* Ep. xi. § 14) mocks at Behrens' account.

[§] Strack, *Journal de Médecine*, 1768, t. xxviii. p 163.

the right side only, but in two weeks it spread over the whole body.[*] This observer surely possessed as good means of forming an opinion on this point, as anyone at the present day. The appearance must, however, be extremely uncommon, one of the rarest phænomena in medicine. Peter Frank says he has never seen such a thing, and thinks it very hard to explain;[†] in which every one who is able to form an opinion on the matter must agree with him. Pouzol attempts to explain it by bringing into notice the varying vascular supply of different parts of the skin, which would cause a like variation in the supply of bile pigment.[‡] This may serve to explain some cases of a yellow colour in spots (*icterus variegatus*); these have, however, still to be proved to be jaundice. It does not explain the appearance of jaundice in one half of the face while the other half remains natural. Morgagni can only explain Behrens' case by supposing a slowness of the circulation in the paralysed side and thus no time being given to tinge the parts.[§]

The older physicians were delighted to enumerate numberless species of jaundice according to the amount of bile pigment present in the skin. Aretæus describes two species, the white and black, *melas icterus*, a word which remains in use in our own day, and says there are myriads of stages between the two.[‖] Many of the so-called species of jaundice are quite different diseases, *icterus albus*, *ruber*, and *cæruleus* being the names for chlorosis, erythema, and cyanosis.

The mucous membranes do not share in the yellow tint of the skin. The lips, for example, retain the redness of health, and the inside of the mouth shows the usual colour.[*] A yellow colour may be seen, however, if pressure be made so as to drive all the blood out of the mucous membrane, and allow the tint which is underneath that of the blood vessels to appear. There is one part of the mucous membrane of the mouth, that under the tongue, which is often yellow, almost constantly so, an appearance noticed by Hippocrates[†] but to which little attention has been paid. Lonjon thinks that in every case of jaundice the *velum palati* shows a deep and constant yellow colour.[‡] And Pupier says that the roof of the mouth is the first to show the yellow colour and the last to lose it.[§] It is true that the roof, where the bone is thinly covered, usually does show a yellow tint.

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[*] Joseph Frank, *Praxeos Medicæ universa præcepta*, Lips. 1843, Part iii. Vol. ii. Sec. ii. Fasc. i. p. 278.

[†] Peter Frank, *De curand. hom. morb. epitome*, Vienna, 1821, Lib. vi. pars iii. p. 308.

[‡] Pouzol, *Essai sur l'ictère*, *Paris* 1872, p. 63.

[§] Morgagni, *loc. cit.*

[‖] Aretæus, *De causis et signis*, Adams' ed. p. 83.

The secretion of mucous surfaces and those of the glands which open upon mucous surfaces or the skin, saving always the notorious example of the kidneys, do not as a rule contain bile pigment. The saliva is colourless. I have often tested it in cases of severe jaundice without being able to detect any reaction with nitric acid.[‖] In like manner the tears, the sweat, and the milk of jaundiced patients are as colourless as in health. To this statement there are rare exceptions.

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[*] Villeneuve (*Dict. des Sciences méd.* Paris, 1818, Vol. xxiii. p. 405) says the lips become a deep yellow, and Lonjon (*Gaz. méd. de Paris*, 1845, p. 231) that the inside of the mouth is yellow.

[†] Hippocrates, *De morb*. Lib. ii. Cap. xxxviii. Littré's ed. t. vii. p. 54.

[‡] Lonjon, *loc. cit.* Decaisne (*Comptes rendus des Séances de l'Académie des Sciences*, 1871, t. lxxiii. p. 1486) noticed the same appearance in an epidemic of jaundice at Paris.

[§] Pupier, *Gaz. hebd.* 1875, p. 307.

[‖] Mosler (*Berliner klin. Wochenschrift*, 1866, p. 173) could find neither bile pigments nor bile acids in the saliva of the parotid gland from three jaundiced patients. Dr. Samuel Fenwick, indeed, (*Lancet*, 1877, vol. ii. p. 303) says that he has examined the saliva in a large number of cases of jaundice, and, whenever the disease has been recent, that he has found the pigment on evaporation. Nothing is said about any chemical means having been used for the recognition of the pigment, so that the presence of biliary pigment in the specimens examined remains doubtful.

The sweat is the most common exception.[*] The linen near the armpits may often be seen stained yellow as if wetted with the urine. This is certainly the most common place for the sweat to be coloured, although the appearance of colour in other parts has been recorded. Thus in an old case of Chomel's, in a woman subject to epilepsy, jaundice came on; a thick sweat broke out during the fit, and the linen with which they wiped the patient was tinged of a saffron colour.[†] Sir Henry Marsh says that Cheyne had met with a patient whose handkerchief was stained yellow when she wiped her face.[‡] Andral mentions a really curious case in which the stools were white, but the skin and conjunctiva colourless; nevertheless the urine was bilious and the linen used to wipe the sweat off the head was coloured yellow. After death the liver was found softened, not fatty; the cystic and hepatic ducts free from bile and a colourless serous fluid in the gall bladder; nothing unnatural was found in the duodenum.[§] Textural changes, like those in the kidneys, do not appear in the sweat glands. Frerichs figures brownish granules within the glands, but nothing like the great masses of pigment seen in the kidney.[‖]

There are some early notices of a change of colour of the saliva in jaundice,[¶] and one of the best of these we owe to so excellent an observer as John Huxham. A gentleman 40 years old, jaundiced, took overnight, with some other medicines, gr. viii. of calomel. The next day a very green saliva poured out of the man's mouth, exactly like green bile, but thinner. This flow of green saliva lasted 40 hours, and very nearly equalled two quarts in amount. The green colour of the saliva passed into yellow, which lasted another 40 hours and then the salivation disappeared as suddenly as it came on. Huxham does not think it due to the mercury, on account of the smallness of the dose; the patient had before been salivated, apparently without mercury.* But the observer who has paid the most attention to the saliva, whether in health or disease, is undoubtedly Samuel Wright; and he has published the most complete account known of the saliva in jaundice. He says that in jaundice, the saliva is seen in two forms, colourless and coloured, and that the coloured bilious saliva is of various shades, from a golden yellow to a deep olive; it is always abundant, and though it sometimes alternates with that of other secretions, it rarely permanently diminishes until the patient be free from the jaundiced tinge. The salivary glands are usually tinged and of a dull red colour, but they are not painful and they show no signs of active inflammation.† Wright thinks a discharge of bilious saliva may precede, accompany, or even hinder, an attack of jaundice. He gives three cases of coloured saliva, in all of which salivation was present; and in the two first mercury was given; in the third the treatment was by "salines and aperients." The saliva tasted bitter to the patients themselves. Dr. Budd likewise speaks of a case of jaundice in which salivation was caused by mercury, and the saliva was deeply coloured with bile.‡ Since, however, the custom of giving mercury for jaundice has fallen out of use, such cases seem to be less common. Leyden, giving two grains of calomel every three hours, caused a salivation; and with the salivation a distinct yellow appearance of the saliva.[*]

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[*] Noticed by Galen, *De sanitate tuenda*, Lib. iv. Cap iv. Kühn's ed. Lipsiæ, 1823, vol. vi. p. 250. It is, however, only said that the sweat is bitter.

[†] Chomel, *Histoire de l'Académie royale des Sciences*, Année 1737, Paris, 1740, p. 49.

[‡] Henry Marsh, *Dublin Hospital Reports*, 1822, Vol. iii. p. 269.

[§] Andral, *Clinique méd.* Paris, 1839, 4e éd. t. ii. p. 374. Cf. p. 320.

[‖] Frerichs, *Path.-anat. Atlas zur Klinik der Leberkrankheiten*, Tafel i. Fig. 6.

[¶] Nuck, *Sialographia*, Lugd. Batav. 1690. p. 49. Riedlinus, *Lineæ Medicæ*, August. Vindelic. Anni 1697. p. 88.

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* Huxham, *Phil. Trans.* 1724. Vol. xxxiii. p. 63.

† Wright, *Lancet*, 1842-43. Vol. i. p. 559.

‡ George Budd, *On Diseases of the Liver*, London, 1857. Third Ed. p. 469.

The records of a bilious saliva without salivation are rare, a yellow appearance of the buccal mucus being always excepted.[†] There is, indeed, a case of Dr. Hilton Fagge's, in which the saliva just before death had the colour of bile. The patient, a woman, had for six months suffered from a macular syphilide, and for three months from jaundice; she denied having used mercury; but during the 10 days of her stay in Guy's Hospital she had the $\frac{1}{16}$ gr. of perchloride of mercury given three times a day, and on the day before death three grains of calomel. It does not appear that there was any notable salivation.[§] Gubler also shortly mentions a case of syphilis and jaundice in which the saliva was yellow; he does not say that the patient was salivated.[§]

The milk of women suckling sometimes contains bile pigment. This was first proved by means of chemical tests by Gorup-Besanez.[‖] Older cases of a yellow appearance of the milk in jaundice have likewise been recorded.[¶] Hervieux found quite lately, in an epidemic jaundice in the *Maternité* at Paris, that in all the women who were suckling, the milk was coloured yellow.[*] Underwood says that he has met with some striking instances in which women, suckling and jaundiced, have communicated the disease to their offspring, which has not been cured until the child was weaned or the nurse recovered.[†]

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[*] Leyden, *Beiträge zur Pathologie des Icterus.* Berlin, 1866. p. 208.

[†] Andral, *Clinique méd.* Paris, 1839. 4e Édition, t. ii. p. 320.

[‡] Hilton Fagge, *Trans. of the Path. Soc. of London*, 1867. Vol. xviii. p. 136.

[§] Gubler, *Gaz. méd. de Paris*, 1854, p. 215.

[‖] Gorup-Besanez, *Arch. f. phys. Heilkunde*, 1849. Jahrg. viii. p. 719.

[¶] Peter Frank, *De curandis hominum morbis*, Vienna, 1821. Lib. vi. pars iii. p. 305. The vaginal secretion was likewise coloured.
Henry Marsh, *Dublin Hospital Reports*, 1822. Vol. iii. p. 263.
Bright, *Guy's Hospital Reports*, 1836. Vol. i. p. 623.
Wunderlich, *Arch. d. Heilkunde*, 1860. Jahrg. i. p. 35.
Marsh's, Bright's, and Wunderlich's cases are from observations on the mammary gland after death. There are some other cases sometimes set down as instances of bile being present in the milk, which merely show that the milk had from some cause or other a bitter taste. (Ol. Borrichius, in Bartholini *Acta med. Hafniensia*, 1673. Vol. ii. p. 164. Obs. lxii. and *Samml. aus. Abh.* 1792. Bd. xv. p. 121. Note.)

I have never been so fortunate as to see the milk coloured in jaundice. A patient of mine, suckling, who had symptoms of simple jaundice, told me that the milk was coloured green. Yet on some being pressed out of the nipple, no colour was apparent; neither on applying Gmelin's test, could any certain reaction be seen; the layer of milk above the nitric acid became of a dirty yellow, markedly different from the white of the milk, but no play of colours or distinct green was seen. Nor did a green colour develope in the milk after it was kept three days.

As to the other secretions they seem to be very rarely coloured. Heberden is commonly quoted as an authority for the statement that the tears sometimes become yellow; all, however, that he does say is that one man assured him his tears were tinged in a jaundice.[‡] Some French writers speak of the tears in the jaundice of the new-born being coloured; but I think this must be a mistake, the pus of an ophthalmia being coloured yellow and thus thought to be tears.[§]

Sander says that the nurse attending one of his cases which died of acute yellow atrophy, reported that the tears were yellow.[‖] This suffers the same want of proof as Heberden's case, as the doctor himself did not see the tears.

The mucus of the nose has been seen to be yellow by one or two observers ;[*] Joseph Frank says he has seen the secretion of the ears altogether suppressed in jaundice.[†] It is likewise asserted that the vaginal mucus is sometimes coloured.[‡] Bouisson says he has found the semen in the *vesiculæ seminales* manifestly yellow.[§]

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[*] Hervieux, *Union méd.* 1872. t. xiii. p. 610.

[†] Underwood, *A Treatise on the Diseases of Children*, Lond. 1805. Fifth edit. vol. i. p. 27.

[‡] Heberden, *Commentaries*, Lond. 1806. 3rd ed. p. 247.

[§] Billard, *Traité des maladies des enfans nouveau-nés*, Paris, 1828. p. 646.

[‖] Sander, *Deutsche Klinik*, 1860. Bd. xii. p. 33.

The fluids poured into the intestinal tract are likewise devoid of colour in jaundice; otherwise the fæces themselves would be coloured. I am not acquainted with any well authenticated case in which these fluids were coloured; indeed it would be hard to prove the presence of bile pigment in them, apart from the fæces.[‖] Osborne speaks of colourless fæces floating in a bilious fluid,[¶] but this seems to me best explained by supposing an admixture of urine.

Although the mucous secretions remain uncoloured in jaundice while the mucous membranes and glands remain healthy, yet the secretions may become coloured in disease. This has been already noticed in the case of the saliva. Simple catarrh does not seem to beget much change; but the croupous exudations are very liable to be coloured in jaundice. For example, in simple catarrh of the bronchial tubes, the mucus is rarely coloured, although I have met with such an instance in one case; yet in pneumonia complicated with jaundice, where a croupous exudation takes place, the sputa are very commonly coloured.

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[*] Kercksig, Hufeland's *Journal*, 1799. Bd. vii. Stück iii. p. 98. There is also an old case by Riedlinus, *Lineæ med.* anni 1697. August. Vindel. p. 88.

[†] Joseph Frank, *op. cit.* p. 282.

[‡] Peter Frank, *De curand. hom. morb.* Viennæ, 1821. Lib. vi. Pars iii. p. 305.
Reclus, *Gaz. des Hôp.* 1872. p. 259.
Stokes, *Lond. Med. and Surg. Journal*, 1834. vol. v. p. 199.

[§] Bouisson, *De la bile*, Montpellier, 1843. p. 151. A similar instance is quoted by Joseph Frank (*op. cit.* p. 281.) from Petermann (*Obs. Med.* Dec. 1. No. 9.)

[‖] Bouisson (*de la Bile*, Montp. 1843, p. 150) says that Voigtel (*Handb. d. path. Anat.* Halle, 1804, Bd. i. p. 552) records a case in which the pancreatic fluid was yellow in jaundice. What Voigtel does say is that a yellow fluid was found in the pancreas of a jaundiced person.

[¶] Osborne, *Dublin Quarterly Journal*, 1853, vol. xv. p. 106.

The fluid exudations into the serous cavities are among the first to show the presence of bile pigment.

The extra-vascular tissues are not coloured in jaundice. There are old stories quoted of the hairs sometimes changing colour; which on examination do not bear out the purpose for which they are brought forward: the case quoted by Schenck suggests chlorosis rather than jaundice;* and Riedlinus' is simply that a jaundiced woman told him that whenever she pulled out a hair, a yellow drop appeared at the spot whence the hair came out.† Stokes, however, tells us that one of his friends considered that the hairs were unquestionably coloured in some cases of jaundice. It does not seem that Stokes had ever seen such cases.‡ Neither have I.

Huxham's statement that the teeth were coloured green for a fortnight after convalescence in his case of bilious saliva§ is confirmed by Wright, who says that in like cases he has seen the teeth coloured permanently yellow, green, brown, or black according to the amount of bile present in the saliva.‖ Thomas Bell says he has seen more than one example of the injection of a tooth with bile in cases of jaundice.¶ It would seem from Bell's statement that only one tooth was coloured among many. The rule in jaundice is that the teeth look uncommonly white from contrast to the surrounding coloured tissue, as the teeth of a negro do.

There is a curious case mentioned by Bleicher, of a man aged 40 who on the 8th day of a jaundice with fever, passed blue urine; and at the same time the lips, tongue, and teeth, became blue. Eight days after he was cured.[*]

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* Schenck, *Obs. med.* Lib. iii. de ictero, Obs. i. Lugduni, 1644, p. 405. Quoted from Cornelius Gemma, Comoscrit. lib. i. cap. 7.

† Riedlinus, *Lineæ med.* Anni 1697, August. Vindel. p. 88.

‡ Stokes, *Lond. Med. and Surg. Journal*, 1834, vol. v. p. 199.

§ Huxham, *Phil. Trans.* 1724, vol. xxxiii. p. 64.

‖ Wright, *Lancet*, 1842-43, vol. i. p. 562.

¶ Thomas Bell, John Hunter's *Works*, Palmer's ed. London, 1835, vol. ii. p. 19, note.

Pain is not a complication of jaundice. Jaundice caused solely by the pressure of a tumour upon the hepatic ducts, or by a plug of mucus within them, is not accompanied by any pain due to the jaundice: if pain be present it is due to some other complication of the disease. It is, however, otherwise when the jaundice is due to the passage of a rough angular gall stone down the ducts; the friction and forcible dilatation of the ducts sometimes cause agony so great that it is needful to give the patient chloroform to remove the pain.

Pouzol, speaking of the slight troubles and absence of pain which in general accompany jaundice, says that he has noticed a headache sometimes attend this disease: the headache is frontal or general, sometimes lancinating, sometimes giving a feeling of weight.[†] This is probably bilious in origin.

Patients with jaundice appear to me to be drowsier than others. They often sleep much during the day. Sleeplessness, unless due to the itching, is not at all a common symptom, although spoken of as one.[‡]

Heberden speaks of hiccup being seen in jaundice, but without denoting any present or future mischief.[§]

Symptoms of disordered digestion are seen in cases of jaundice complicated with signs of gastric catarrh; that is, a large proportion of cases. But in many cases of chronic jaundice, digestion seems to suffer but little. The appetite is good and the tongue remains clean. Frerichs states that the patients suffer from much flatulence, due to the want of bile in the intestine.[‖] Curiously enough, Hippocrates says precisely the reverse, that the jaundiced are not at all flatulent;[*] and in my experience of chronic jaundice it has not been at all a prominent symptom. There seems to be a dislike to fat. Those who in health have eaten and liked fat, when jaundiced, refuse it. Budd describes a patient who had, at times, a voracious appetite, with a craving for oysters and small shell-fish, which even in large quantities, never disagreed.[†]

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[*] Bleicher, Schmidt's *Jahrbb.* 1839, Bd. xxi. p. 48.

[†] Pouzol, *Essai sur l'ictère*, Paris, 1872, p. 78. Portal (*Maladies du foie*, Paris, 1813, p. 133) says shortly that heat and weight of the head are often seen in jaundice.

[‡] Pouzol, *loc. cit.*

[§] Heberden, *Commentaries*, Lond. 1806. Third ed. p. 246.

[‖] Frerichs, *op. cit.* Bd. i. p. 118.

The blood early suffers in jaundice. Saunders showed that, within two hours after ligature of the bile duct, the blood gave evidence of the presence of bile pigment.[‡] I have repeated this experiment, following Saunders' directions exactly, but without attaining his results.[‡] Frerichs in like manner, could only detect bile pigment in the blood at the end of 48 hours after the ligature of the ducts.[§] I quite agree, however, with his statement that bile pigment may be found after death in the serous effusions of the chest or belly in cases where none can be detected in the urine, or any change of colour seen in the skin. I have several times verified this statement, taking care to use only the fluids from the chest, as it may be objected to those from the belly that the bile in the gall bladder may have transuded after death.

It is granted by all that the bile pigments exist in the blood in jaundice.[‖] The same cannot be said of the bile acids. For many years a fruitless search was made for them, only one chemist[*] since Pettenkofer's discovery, and that not in cases of disease of the liver, being able to find their peculiar reaction in the blood. In 1858 came Hoppe-Seyler's discovery of the bile acids in the urine[†] and Kühne soon after found them in the blood of jaundiced dogs, even so soon as 24 hours after complete occlusion to the ducts.[‡]

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[*] Hippocrates, *Aphorisms*, Section v. § 72. Littré's ed. t. iv. p. 562. *Οἱ ἰκτεριώδεες οὐ πάνυ τι πνευματώδεές εἰσιν.*

[†] Budd, *On Diseases of the Liver*, London, 1857, third ed. p. 219.

[‡] Saunders, *A Treatise on the Structure, Economy, and Diseases of the Liver*, London, 1803, 3rd ed. p. 111.

[‡] Wickham Legg, *St. Bartholomew's Hospital Reports*, 1873, vol. ix. p. 176.

[§] Frerichs, *op. cit.* Bd. i. p. 99.

[‖] See Lecanu, *Transactions méd.* 1831, t. vi. p. 113, note, for the bibliography of the older researches into the presence of the colouring matter of the bile in the blood. I have looked through these references, but the authors do not communicate any important results. Kane (*Dublin Journal*, 1833, vol. ii. p. 346) confirms Lecanu's statements.

Huppert found them in the blood of a rabbit who lived only six and a half hours after the bile ducts were tied, and in the blood of a cat who lived more than sixteen hours after.[§] Also in the blood of a man who died of acute yellow atrophy. But Ernst Bischoff could not find them in the blood, muscles, brain, or cerebro-spinal fluid of a patient who died with intense jaundice from cancer of the liver.[‖]

When it was the custom to make analyses of the blood in mass, analyses to which little regard is now paid, several examinations of the blood from jaundiced persons were made. Lecanu[¶] and Simon[**] found the amount of colouring matter of the corpuscles decreased, while Denis[††] found the globules natural in amount, but the albumen decreased. Gorup-Besanez[‡‡] found an increase of the water, and decrease of the blood-corpuscles; and, at the same time no increase of fatty matters, and no cholestearin. The absence of any increase of fat or cholestearin was noticed also by Kane* and Simon†. On the other hand Becquerel and Rodier found an increase in the fatty matters and cholestearin;‡ Frerichs, a large increase in the fatty matters, which were rich in cholestearin, and which rose sometimes to 4 or 5 *per cent*. Leucin was also found in the blood.§

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[*] C. G. Lehmann, *Lehrb. d. phys. Chem.* Leipzig, 1853, 2te Aufl. Bd. i. p. 122. Jac. Moleschott (*Zeitschrift f. rat. Med.* 1847, Bd. vi. p. 387) thought he detected bilin, *i.e.* the bile acids in the blood in a case of "hepatitis."

[†] For history of this, see the section on the urine.

[‡] Kühne, *Arch. f. path. Anat.* 1858, Bd. xiv. p. 347.

[§] H. Huppert, *Arch. d. Heilk.* 1864. Jahrg. v. p. 253.

[‖] Ernst Bischoff, *Zeitschrift f. rat. Med.* 1864, iii. Reihe, Bd. xxi. p. 142.

[¶] Lecanu, *Trans. méd.* 1831, t. vi. p. 109. The blood which he examined did not clot till long after it had cooled.

[**] Simon, *Animal Chemistry*, Day's Trans. 1845, vol. i. p. 330.

[††] Denis, *Essai sur l'application de la Chemie à l'étude physiologique du Sang*, Paris 1838, p. 309.

[‡‡] Gorup-Besanez, *Arch. f. phys. Heilk*, 1849, Bd. viii. p. 530.

Dr. Samuel West found, "in a case of severe jaundice, probably depending on gall stones, the patient being in a state of the most extreme anæmia, and so weak that the least exertion caused fainting," that the blood showed the following characters: "The cells were considerably diminished in number, and the blood very watery. The red cells did not form rouleaux, were much diminished in size, hardly half as large as a healthy red cell, most irregular in shape, and deeply coloured, resembling the bodies described by Lebert as tubercle corpuscles. The white cells were in relative excess. In this one particular only did the blood in the case differ from that described in idiopathic or pernicious anæmia. The patient, however, recovered, and with his improvement, his blood gradually returned to its normal condition; and on his leaving the Hospital this note is recorded: Red blood cells nearly natural again; here and there one still misshapen. They form rouleaux; the white are no longer in excess."‖

Budd, though he seems to have made no analyses, says that, after jaundice has lasted some time, the globules of the blood are always less in proportion than in health. This probably results, not so much from the mere presence of the principles of the bile in the blood as from a diminution of those reparative changes which the blood naturally undergoes in its passage through the liver, and to the impaired digestion which results from the absence of bile in the bowel.[*] Leyden seems to incline to believe that the poverty of the blood is due to the action of the bile acids upon the corpuscles.[†] For my own part, I feel disposed to agree with Budd and attribute the state of the blood to the impaired action of the liver and the impaired nutrition rather than to the solvent action of the bile acids upon the corpuscles.

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* Kane, *Dublin Journal*, 1833, vol. ii. p. 346.

† Simon, *loc cit.*

‡ Becquerel and Rodier, *Recherches sur la composition du Sang*, Paris, 1844. p. 106.

§ Frerichs, *op. cit.* Bd. i. p. 103.

‖ Samuel West, *St. Bartholomew's Hospital Reports*, 1877, vol. xiii. p. 218.

The fæces in jaundice are often entirely wanting in colour.[‡] They have a grey or clay coloured appearance, and are less consistent than the stools seem in health. Frerichs, however, says that the stools are firmer and more consistent.[§] To this statement, I fear, I cannot assent; or to that, that constipation is the rule. In simple jaundice, which is, I suppose, the most common of all kinds of jaundice, diarrhœa is very often seen. In chronic jaundice, diarrhœa is less common. In this statement I am supported by no less profound an observer than Heberden; who, granting that costiveness might be looked for in jaundice, as the irritation from the bile is wanting, says that in fact icteric persons are often disposed to have a purging. He looks upon the diarrhœa as a help to distinguish jaundice from ileus.[‖]

Sometimes the fæces are particoloured; some part being more deeply stained with bile than the other; or even one part free from bile altogether, while the other is coloured. Graves explains this appearance by supposing that the liver secretes bile during a certain part of the digestive process, then stops, and then secretes again.* It is rare in jaundice for the fæces to be unchanged in colour, or to show more staining with bile than natural. This last has given rise to theories of polycholia, or an excess of bile, as a cause of jaundice; and is one of the points relied upon by the defenders of the theory of hæmatogenous jaundice. Doubtless the appearance of highly coloured fæces is sometimes hard to explain upon the theory of an obstruction to the duct if the admixture of foreign colouring matters, such as blood or drugs, can be disproved. Still it is well to keep in mind the facts disclosed by morbid anatomy: some of the small ducts may be obstructed high up in the liver, while the large ducts and branches leading into them are quite free; also the small amount of colouring matter that need be in the blood to bring about the appearance of jaundice.

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[*] Budd, *On Diseases of the Liver*, London, 1857, 3rd ed. p. 468.

[†] Leyden, *Beiträge zur Pathologie des Icterus*, Berlin, 1866, p. 117.

[‡] Hippocrates describes the stools as yellow-white and stinking. (*De morb. int.* Cap. xxxv. Littré's ed. t. vii. p. 252.) Aretæus says that their want of colour is due to absence of bile. (*On the Causes and Symptoms of Chronic Diseases*, Book 1. Chapt. xv. Adams' transl. p. 324.)

[§] Frerichs, *op. cit.* Bd. i. p. 119.

[‖] Heberden, *Commentaries*, Lond. 1806. Third ed. p. 246. The same opinion is expressed by Powell. (*Observations on the Bile and its diseases*, London, 1800, p. 85.

If the fæces be colourless, there can be little doubt that no bile enters the intestine; in other words, that the obstruction of the bile duct is complete. But the contrary does not hold good. The fæces may owe their colour to other sources than the bile; as the administration of drugs, like charcoal, bismuth, or iron. Likewise the appearance of hæmorrhages into the intestinal tract in jaundice is far from uncommon, and blood mixed with the stools may readily give the deceptive appearance of a dark or brown colour to the fæces. I cannot, however, agree with Osborne that it is possible that the secretions from the bowels may be coloured while the fæces are white. He says that the fæces in jaundice may be seen to be of a white colour like putty, surrounded by a green or yellow liquid.† This seems to me to be due possibly to some error of observation. The fæces may not unfrequently be seen surrounded by a coloured liquid, but this is in cases where the bilious urine has been suffered to mix with the uncoloured stools, and thus a deceptive appearance caused.

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* Graves, *Clinical Lectures on the Practice of Medicine*, Dublin, 1864, p. 342. Reprint ot second ed. edited by Neligan.

† Osborne, *Dublin Quarterly Journal*, 1853, vol. xv. p. 106.

The fæces in jaundice do not seem to have been examined with much attention by the chemists.[*] Dr. Austin Flint, the younger, has found that they contain no stercorin,[†] a substance, which he says, is derived from the decomposition of cholestearin, and which always appears in natural fæces. Dr. Flint thinks that no cholestearin is found in natural fæces. Hoppe-Seyler commenting on Dr. Flint's researches says that stercorin is nothing more than an impure cholestearin; cholestearin itself being abundantly found in the fæces of mammalia, including man.[‡] A large amount of fat was also found by Dr. Flint in the fæces of jaundice: Farines, in an old analysis, found the greater part of the fæces in jaundice to be formed of a fatty matter, soluble in æther.[§] A like result was attained by Trommer, who analysed the fæces of one medical student who was jaundiced, and compared the results with those obtained from the fæces of another medical student, who was healthy, but ate the same food. Far more fat was found in the fæces of the former than of the latter.[‖] Jaundiced persons, it is well known, dislike fat.

The Urine. The urine very early shows changes in jaundice. It becomes highly coloured.[¶] Linen or white paper dipped into it is stained yellow. This is an appearance often noticed by the patients themselves. The froth on the surface shows a yellow look and is long in disappearing.

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[*] See Hoppe-Seyler, *Phys. Chemie*, Berlin, 1878, p. 358.

[†] Austin Flint, *Recherches exp. sur une nouvelle fonction du foie*, Paris, 1868, p. 101; also in *American Journal of the Medical Sciences*, 1862, vol. xliv. pp. 358 and 364.

[‡] Hoppe-Seyler, Virchow's *Jahresbericht f.* 1868, Bd. i. p. 97.

[§] Farines, in Orfila, *Elém. de chimie appliquée à la méd. et aux arts*, Paris, 1836, t. iii. (Quoted by Bouisson, *de la Bile*, Montpellier, 1843, p. 151.)

[‖] Trommer, reported by F. von Niemeyer, *Text Book of Practical Medicine*, trans. by Humphreys and Hackley, New York, 1870, Vol. i. p. 679.

[¶] The change in colour was noticed by Hippocrates (*De aff. int.* Cap. xxxv. Littré's ed. t. vii. p. 252 *et seqq.*)

The colour may be scarcely darker than natural, and need a chemical test to show the presence of bile: or the urine may be almost as dark as porter, of a green brown, or brown black. The reaction is acid, and the specific gravity is not low, seldom falling below 1010.[*] The urine is commonly clear; but may sometimes be turbid owing to the presence of urates, apparently not dependent upon the temperature of the patient.

The quantity of urine passed in the 24 hours in jaundice is subject to considerable variations. Becquerel found in three cases in which he carefully noted the appearances of the urine that in the first, a man, the amount in 24 hours was 1419.C.C.; in the second, a man jaundiced after a violent dispute, it was 634.C.C. and in a third, a pregnant woman, it was 640.C.C.[†] The observations, however, were only made on one day, and are therefore less valuable than those which follow and which were made in succession. Leyden found in one of his cases that the urine was increased in quantity while the temperature was normal, but sank in amount during a paroxysm of fever.[‡] A. Vogel found in his case of jaundice lasting for many months, and due to cancer of the liver, that the amount of the urine varied from 1350.C.C. to 2000.C.C.[§] Kölliker and Müller in their observations on a woman of 25, suffering from simple jaundice found that the mean amount of the urine during the jaundice was 1670.C.C.; during the convalescence 1401.C.C.; when quite well 1370.C.C.* So that in this case there seems some evidence that the amount of urine passed was really increased in amount.

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[*] Gorup-Besanez (*Arch. f. phys. Heilkunde*, 1849, Jahrg. viii. p. 713) says that the specific gravity of the urine of jaundice is commonly high, about 1031.

[†] Becquerel, *Séméiotique des Urines*, Paris, 1841, pp. 413 and 393.

[‡] Leyden, *Beiträge zur Path. des Icterus*, Berlin, 1866, p. 205. He likewise gives cases of increased or abundant flow of urine at pp. 114 and 184, although in the former of these two the temperature was high.

[§] A. Vogel, *Zeitschrift f. rat. Med.* 1854, Bd. iv. (neue Folge) p. 391.

Julius Jacobs found the amount in three cases to be 2409.C.C. 1638.C.C. and 1332.C.C.†

In four cases examined by Valmont the amount was found rarely to rise above 1000 C.C. One of these was believed to be a case of cancer of the liver; in the other three, cirrhosis was diagnosticated; and in two, verified after death.‡

I have measured the amount of urine passed in the 24. hours in ten cases of jaundice due to various causes. The highest mean was in a case of complete obstruction to the ducts by a hydatid cyst, and equalled 2790 C.C. in the twenty-four hours. The lowest mean was in a case of cancer of the pancreas and liver and equalled 570. C.C. In two other cases of jaundice due to the same cause the mean were 1971. and 1120. C.C. In the remaining six cases the means of the urine passed were 1100, 1355, 1433, 1481, 1788, and 2234. C.C. amounts not above or below the standard of health§

In some cases of jaundice it has been noticed that, as the patient was dying, the amount of urine passed become very small, or indeed sank almost to nothing. Such a case has been noticed by Devay in which the urine was suppressed three days before death after a 7. years' jaundice from gall stones.*

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* Kölliker und Müller, *Verhandlungen der phys. med. Gesellschaft in Würzburg*, 1856, Bd. vi. p. 497.

† Julius Jacobs, *Arch. f. path. Anat.* 1877, Bd. lxix. p. 487.

‡ Valmont, *Étude sur les causes des variations de l'urée dans quelques maladies du foie*, Thèse de Paris, 1879, p. 36 *et seqq.* See also Vulpian, *Clinique méd. de l'Hopital de la Charité*, Paris, 1879, p. 253.

§ Wickham Legg, *Med. Chir. Trans.* 1876, Vol. lix. p. 149. Dogs, whose bile ducts have been tied, pass a greatly increased quantity of urine. Tiedemann and Gmelin (*Recherches expérimentales sur la digestion*, Paris, 1827, Partie ii. p. 47) also noted that the urine was abundant. Feltz and Ritter found that after the injection of bilirubin into the veins, the amount of urine was much increased. (Robin's *Journal de l'Anat. et de la Phys.* 1875, t. xi. p. 155.

Albumen is rarely absent from jaundiced urine. The amount is indeed small, and some care is needed to detect it. No cloudiness is given by heat, as a rule; but opalescence, however, appears on dropping a little nitric acid into the boiling urine. I look upon this as evidence of the presence of albumen in the urine. No white ring is commonly formed where a layer of nitric acid touches the urine.

According to Kühne, the cause of the presence of this small quantity of albumen in jaundiced urine would be due to the action of the bile acids upon the red corpuscles.† It is well known that the red corpuscles, wherever they come in contact with the bile acids, are dissolved. Free hæmoglobin thus becomes present in the plasma of the blood, and is thrown out by the kidneys. The bile acids must be present in but small quantity in the blood, or a much larger amount of albumen would be thrown out by the kidneys.

Sugar is not often met with in jaundiced urine. Indeed though I have carefully looked for it in nearly all the cases which I have examined, I have never met with it. The test which I have used has been Trommer's. On theoretical grounds the appearance of sugar should be rare, as one important form of diabetes does seem to arise from the liver. I have shown that after ligature of the bile duct glycogen disappears in the liver, and that when the fourth ventricle is irritated under the same circumstances, no sugar appears in the urine.‡ So in jaundice if the obstruction to the ducts be complete, no sugar from the liver should appear in the urine. There are, however, a few cases in which sugar has appeared in the urine of jaundice. In Golowin's case, a dog was artificially jaundiced, and each time that milk was given to the animal, sugar appeared in the urine.[*]

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* Devay, *Gaz. méd. de Paris*, 1843, p. 263, Cf. Frerichs, *op. cit.* Bd. i. p. 147.

† Kühne, *Lehrb. d. phys. Chemie*, Leipzig, 1868, p. 545.

‡ Wickham Legg, *St. Bartholomew's Hospital Reports*, 1873, Vol. ix. p. 161, and *Arch. f. exp. Path.* 1874, Bd. ii. p. 384.

Valmont has, however, given 150 or 200 grammes of *sirop de glucose* to patients suffering from jaundice, and not been able to detect any sugar in the urine passed afterwards.[†] In some cases of an advanced cachexia, he says that he found the sugar again, but with large doses it is possible to cause glycosuria even in healthy people.

There is an important case of diabetes recorded by Dr. Bright, in his paper on diseases of the pancreas. A man, 49 years of age, first felt symptoms of diabetes in the month of March. In the beginning of September he began to be jaundiced; and at the end of December, the sugar had disappeared from the urine. The man died on March 1st, and the common duct was found to end in a *cul de sac* in the diseased substance of the pancreas, complete obstruction having taken place.[‡] The theory of this case would be that the gradual obstruction of the ducts caused the liver to cease its glycogenetic function, and the diabetes also to end: while at last the patient died from the effects of the jaundice.

Frerichs has reported the following case. After death the head of the pancreas was found enlarged and completely obstructing the ducts. Old capillary apoplexies were found in the *pons Varolii.* The man was 50 years old and began to be yellow in December. No suspicion of diabetes seems to have been aroused until about March 15th, when it was discovered that the patient was passing sugar. The quantity was never more than 5000 C.C. in the 24 hours and the specific gravity varied from 1009 to 1018. The amount of sugar was estimated by Soleil's polarisation apparatus, and varied from ·822 to 2·88 *per cent.* Three days before death the sugar disappeared from the urine, and after death none could be found in the substance of the liver.* Dr. George Harley says that on two occasions he found a little sugar in the urine of a jaundiced man,† but he does not give his method of testing.

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[*] Golowin, *Arch. f. path. Anat.* 1871, Bd. liii. p. 428.

[†] Valmont, *Étude sur les causes des variations de l'urée dans quelques maladies du foie*, Thèse de Paris, 1879, pp. 24, *et seqq.*

[‡] Bright, *Med. Chir. Trans.* 1833, Vol. xviii. p. 3.

It is a matter of doubt among physiological chemists whether the bile pigments be not natural constituents of the urine. It is acknowledged generally that they may be found in the urine of healthy men in summer weather, after much drink, long-fasting, &c. In the urine of many animals, such as dogs and cats, there is a substance almost always present which closely imitates the reaction of bile pigment with nitric acid.

The best way of testing for bile pigment in the urine is as follows: ordinary nitric acid, in which some nitrous acid is nearly always present, is poured into a test tube for the depth of an inch. On to the surface of this the urine to be tested is gently poured by means of a pipette, down the side of the tube, so that the two fluids may touch, but not mix. A red line forms at the place of contact in every urine. If the urine contain bile pigment, however, a zone above becomes green, then blue, violet, and lastly red, the uppermost ring being green. This colour is certainly the most characteristic, and without it, the reaction must always be thought dubious. In most bilious urines only the green colour is seen. The varying shades of colour answer to the stages of oxydation of the bile pigment. The reaction is known by the name of Gmelin.

Fleischl says that it is now common to practice Gmelin's reaction according to a modification of Brücke's.[*] To pure nitric acid, obtained by boiling, concentrated sulphuric acid is cautiously added. The sulphuric acid from its great specific gravity falls to the bottom. It hinders the too rapid developement of the colours, and the reaction gradually spreads upwards from the line of union of the two fluids, instead of taking place simultaneously throughout the liquid; all the different colours may be seen one above the other. Instead of pure nitric acid, a solution of nitrate of sodium may be used.[†]

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* Frerichs, *op. cit.* Bd. i. p. 153.

† George Harley, *Jaundice*, London, 1863, pp. 78 and 79.

Carefully practised, it is by far the best test for bile pigment.[‡] Other methods have been proposed, as that of Maréchal, who mixes two or three drops of tincture of iodine with the urine, and finds an emerald green colour given to the fluid.[§] This test, however, is lacking in delicacy. It is hard to perceive the green colour when the amount of bile pigment is small, though easy to find when the colour of the urine is so deep as not to be mistaken for anything else but bilious urine. At the beginning and end of an attack of jaundice the iodine often fails when the nitric acid gives a distinct green. Dr. Walter Smith, however, thinks it a delicate reaction.[‖]

Another test for the presence of bile pigment has been lately brought forward, *violet de Paris*, or methylanilin violet. It appears, however, that the reaction seen equally well with urine coloured with senna or rhubarb, or by the carbolic acid treatment. It is thus worthless for the purpose for which it has been introduced.[*]

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[*] Brücke, *Sitzungsberichte d. math.-naturw. Classe d. k. Akad. d. W.* Wien, 1859, Bd. xxxv. p. 14. Brücke himself advises dilute nitric acid.

[†] Fleischl, *Chem. Centralblatt*, 1875, p. 568 from the *Journal of Chemical Society*.

[‡] Rosenbach (*Centralblatt f. d. med. Wissenschaften*, 1876, p. 5) proposes a modification of Gmelin's test. Some of the urine is filtered through filtering paper and then a drop of nitric acid let fall on the paper as it lies in the funnel. A fine green circle is developed.

[§] Maréchal, *Journal de Pharmacie et de Chimie*, 1869, 4e Série, t. ix. p. 189.

[‖] Walter G. Smith, *Dublin Journal of Medical Science*, 1876, Vol. lxii. p. 449.

Ultzmann also recommends the following method: 10 C.C. of the urine are mixed with 3 or 4 C.C. of a 33 *per cent.* of caustic potash solution. The mixture is then acidified with pure hydrochloric acid: a beautiful emerald green colour is seen if bile pigment be present.[†]

Städeler believes that the chief pigment in jaundiced urine is biliprasin; because the urine becomes green with acids and brown with alkalies, and solutions of biliprasin show like reactions.[‡] On the other hand, Schwanda, from numerous observations, asserts that bilirubin is the chief pigment in jaundiced urine, and that only traces of biliprasin can be found, so that it is the bilirubin which is the chief cause of colour, not biliprasin.[§] Städeler's test is not nearly so delicate as Gmelin's. It is useful sometimes in determining if the high colour of the urine be due solely to drugs. Rhubarb and santonin both give a high colour to the urine, hardly to be distinguished by the eye from that of jaundice. Alkalies, however, deepen to a red the urine passed after rhubarb and santonin, but give a brown colour to the urine of jaundice.

Schwanda has attempted the estimation of the bilirubin passed in the urine, and if his results may be trusted, the amount is extremely small, even in cases where the urine is deeply coloured. The greatest amount found was ·015 grm. in the 24 hours. In one case it was as little as ·002 grm.[||] Thus the largest amount which the urine contained was one part of bile pigment in 100,000 parts of urine. Even if these results be only approximately true, the amount of pigment passed must be very small in comparison with the pigment excreted in health by the liver.

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[*] Gubler, *Gaz. hebd.* 1876, p. 332. See also p. 9 of the same journal.

[†] Ultzmann, *Centralblatt f. d. med. Wiss.* 1877, p. 831.

[‡] Städeler, *Annalen d. Chem. u. Pharm.* 1864, Bd. cxxxii. p. 341. According to Städeler, the formula for biliprasin is $C^{32}H^{22}N^{2}O^{12}$; for bilirubin, $C^{32}H^{18}N^{2}O^{6}$. Maly suggests that biliprasin and biliverdin are identical. (*Journ. f. prak. Chem.* 1868, Bd. civ. p. 32.)

[§] Schwanda, *Wiener med. Wochenschrift*, 1865, p. 692.

[||] Schwanda, *op. cit.* p. 989.

In some cases of jaundice, even when the urine is high coloured and clearly contains abundance of some kind of pigment, no reaction, or no distinctive reaction, with nitric acid can be seen. Prussak believes that this absence of reaction is due to the presence of fever, and that the bile pigments are burnt off or oxydised in the blood so that they can no longer be detected in the urine.[*] Huppert, again, says that in many cases of jaundice, no pigment but biliprasin can be found during the whole course of the disease, and it is to the absence of any other pigment but biliprasin that the trouble in applying the nitric acid test is due.[†] These two statements are not contrary, as biliprasin is but a more highly oxydised body than bilirubin; yet Städeler affirms that biliprasin gives all the reactions of bile pigments with nitric acid, saving only that the blue colour is indistinct.[‡] Frerichs likewise attributes the failure of the nitric acid reaction to an oxydation either in or out of the body.[§] Nitric acid only gives in this case a red colour.

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[*] Prussak, *Centralblatt f. d. med. Wiss.* 1867, p. 97.

[†] Huppert, *Arch. d. Heilkunde*, 1867, Jahrg. viii. pp. 351 and 476. This writer finds the best plan of recognising even traces of bile pigment in the urine is to precipitate with milk of lime, let the mixture stand, and filter. Some of the precipitate, the size of half a hazel nut, is put into a test tube, and the test tube half filled with absolute alcohol, and dilute sulphuric acid added till the fluid have a distinct acid reaction. A precipitate is slowly thrown down of a greenish colour; and if the fluid be gently warmed, the alcohol itself becomes of a greenish colour. Hilger recommends that 50 to 100 C.C. of the urine be gently warmed, and hydrate of baryta added until an alkaline reaction appear. The precipitate is collected and washed: if sprinkled with nitric acid the well-known colours are seen. Or the precipitate may be heated with solution of carbonate of soda, when the pigments pass into the solution, and it acquires a green or brownish-green colour. (Hilger, *Journal of Chemical Society*, 1876, Vol. i. p. 445.)

[‡] Städeler, *loc. cit.*

[§] Frerichs, *op. cit.* Bd. i. p. 106.

Lewin states that, when jaundiced urine gives no reaction with nitric acid, the reaction may sometimes be seen on cooling the urine with ice, thus causing a precipitation of the urates, collecting the urates on a filter, dissolving them in warm water, and testing this solution with nitric acid. A beautiful Gmelin's reaction may thus be seen.[*] These observations closely agree with those of Ernst Bischoff, who found a large amount of pigment thrown down with the uric acid after acidulation.

Although the presence of one element of the bile, the pigment, is plain almost to the unaided senses without chemical help, yet it is quite otherwise with another important element of the bile, the conjugate acids. Before the days of Pettenkofer[†] and Strecker[‡] it was well nigh hopeless to search for these crystalline elements of the bile in the urine. Nevertheless some observers thought they had detected them both in the blood and urine of jaundice. After Pettenkofer, none succeeded[§] in finding the bile acids in the urine, notwithstanding many attempts by observers in every way worthy of credit. It was therefore assumed that the bile acids were absent from the urine in jaundice, and it became a matter of importance to explain their absence. Frerichs and Städeler found that after the injection of colourless bile into the veins of animals, the urine was tinged of a high colour, and gave a well-marked reaction with Gmelin's test, showing the presence of bile pigment[‖] and yet no bile acids could be found in this urine. The same observers afterwards found that when sulphuric acid was allowed to act upon the bile acids, a coloured substance was seen, which gave with nitric acid the same play of colours as bile pigment.[*] Here there seemed a clear way out of all difficulties. The bile acids do not appear in the urine, because they are oxydised in the circulation into bile pigment.

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[*] Lewin, *Centralblatt f. d. med. Wiss.* 1875, p. 81.

[†] Pettenkofer, *Annalen d. Chemie u. Pharm.* 1844, Bd. lii. p. 90.

[‡] Adolph Strecker, *ibid.* 1848, Bd. lxv. p. 1.

[§] C. G. Lehmann, however, says (*Lehrb. d. phys. Chemie*, Leipzig, 1853, 2te Aufl. Bd. i. p. 122.) that he has found substances, which give Pettenkofer's reaction, in the blood and urine of persons whose livers did not seem immediately concerned in the disease.

[‖] Frerichs, *op. cit.* Bd. i. p. 404. I have elsewhere (p. 235.) remarked npon the incorrectness of this observation.

But in 1858, two years after the publication of this last discovery, Hoppe detected in jaundiced urine a notable quantity of choloidic acid, an acid derived from the bile acids, but containing no nitrogen, and yet giving Pettenkofer's reaction.[†] Later on he demonstrated the presence of nitrogenous derivatives from the bile acids,[‡] and last of all, the presence of glycocholic and taurocholic acids themselves, together with cholalic acid, in the urine of jaundice.[§]

This discovery of the bile acids or their derivatives in the urine was soon after confirmed by Kühne,[||] and although at first doubted by some,[¶] yet these acids have been so repeatedly found by those who have used Hoppe's improved method of searching for them, that their presence in the urine of jaundice is now generally admitted.

It may be doubted if the total amount of bile acids in the urine have ever been properly estimated. It is at all events so small that Pettenkofer's test applied directly to the urine gives no certain result. Hoppe in a case of acute yellow atrophy found about ·03 *per cent.* of cholonic acid;[**] and Ernst Bischoff gives as the result of three estimations, ·02, ·04, and ·05 *per cent.*

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[*] Frerichs and Städeler, *Arch. f. Anat. Phys. &c.* 1856, p. 55.

[†] Hoppe, *Arch. f. path. Anat.* 1858, Bd. xiii. p. 101.

[‡] Idem, *ibid.* 1862, Bd. xxiv. p. 1.

[§] Hoppe-Seyler, *Centralblatt f. d. med. Wiss.* 1863, p. 337.

[||] Kühne, *Arch. f. path. Anat.* 1858, Bd. xiv. p. 315.

[¶] Neukomm, *Arch. f. Anat. Phys. &c.* 1860, p. 368.

[**] Hoppe, *Arch. f. path. Anat.* 1862, Bd. xxiv. p. 8.

This latter observer looks upon ·3 grm as the *maximum* of bile acids excreted in jaundice by the urine during the 24 hours,* a result which agrees generally with that of Hoppe-Seyler.

If Pettenkofer's test be applied directly to many urines, a reaction follows which may readily be confounded with that seen in a pure solution of bile acids. Sulphuric acid by itself, without the presence of sugar, will often cause a fine red or purple colour, by inexperienced eyes easily to be mistaken for Pettenkofer's reaction. This is most often the case in a high coloured or albuminous urine, and is not uncommon in perfectly natural urine. Nothing therefore but disappointment and utterly untrustworthy results can be looked for from the direct application of Pettenkofer's test to jaundiced urine. It is a method which should never be adopted. The bile acids must be separated out from the jaundiced urine before their presence can be definitely asserted. Neukomm has found that urine to which 1 *per cent*. of bile acid had been added gave with sulphuric acid and sugar a reaction not to be distinguished from that given with sulphuric acid alone by the same urine to which no bile acid has been added. The Pettenkofer's reaction only became unequivocal when the urine contained ·5 *per cent*. an amount greatly exceeding that ever seen in the urine of jaundice.†

To detect the bile acids in jaundiced urine a long preparation is needed. In Hoppe's first experiments, the urine was boiled with milk of lime, then filtered, and again boiled with hydrochloric acid. This undoubtedly causes a large destruction of the bile acids, and the method which is now recommended is as follows: Precipitate the bile acids with acetate of lead from the urine, made faintly ammoniacal: wash the precipitate with a little water, boil it with alcohol, and filter hot. The lead salts of the bile acids are soluble in hot alcohol; a few drops of soda solution should next be added, and the whole evaporated to dryness. This should now be boiled with absolute alcohol, filtered and evaporated to a small volume, and then poured into a great excess of æther. In this way the bile acids may often be crystallised out.*

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* Ernst Bischoff, *Zeitschrift f. rat. Med.* 1864, Bd. xxi. p. 140.

† Neukomm, *Annalen d. Chemie und Pharmacie*, 1860, Bd. cxvi. p. 34.

This process is troublesome, and ill fitted for the wants of the practitioner. Modifications of it have been proposed. A rapid way of testing has been set forth by Strassburg. A piece of filtering paper is dipped into the urine to be tested, to which a little cane sugar has been added. The paper is then dried, and on the centre is let fall a drop of concentrated sulphuric acid. Around the drop of acid a beautiful violet colour forms.† In my own hands, however, this test has proved very unsatisfactory. I have noticed a purplish colour, identical with that seen with jaundiced urine, arise with natural urine, or with urine from patients not known to have anything amiss with their livers.

Hilger recommends a modification of Hoppe-Seyler's method. The urine is mixed directly with basic acetate of lead and ammonia; and the precipitate is then dried at a low heat and again and again warmed with absolute alcohol. The alcoholic extract is decomposed with carbonate of soda, evaporated to dryness, and again taken up by warm alcohol. The bile acid salts are then thrown by æther, in the usual way.‡

By some observers the bile acids are now looked upon as natural constituents of the urine. Naunyn collected large quantities of natural urine and was able to detect an appreciable amount of bile acids by the process of precipitation with lead.[*] Fudakowski[†] Höne[‡] and Vogel have[§] repeated and confirmed these observations, but their value has been doubted by Wolff.[‖]

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* Hoppe-Seyler, *Handb. d. phys.- u. path.-chem. Analyse*, Berlin, 1865, 2te Aufl. p. 274.

† Strassburg, *Arch. f. d. ges. Phys.* 1871, Bd. iv. p. 461. See also p. 5 of this work.

‡ Hilger, *Journal of the Chemical Society*, 1876, Vol. i. p. 445. Another method for recognising bile is given by Casali in *La Scienza applicata*, 1876, I. fasc. 6. quoted in *Centralblatt f. d. med. Wiss.* 1878, p. 583.

The presence of the bile acids in natural urine, if granted, is probably due to an absorption of the bile acids from the intestine, a very small quantity passing through the liver into the general circulation.

It has, however, been asserted of late that in long continued jaundice the liver loses the power of secreting the bile acids, and thus none appears in the urine. Golowin found none either in men or animals.[¶] Huppert found the amount much decreased towards the end of a case of acute yellow atrophy:[**] and Dr. Pye-Smith could find no bile acids in 14000. C. C. of the urine of a patient jaundiced a long time, probably from gallstones.[††]

Neither dyslysin, nor glycocoll or taurin has ever been found free in the urine.[§§] The first is a product of the decomposition of the bile acids; the two last are important constituents of glycocholic and taurocholic acid.

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[*] Naunyn, *Arch f. Anat. Phys. &c.* 1868 p. 430.

[†] Fudakowski, *Centralblatt f. d. med. Wiss.* 1869, p. 129.

[‡] Höne, *ibid.* 1874, p. 872.

[§] Vogel, Schmidt's *Jahrbb.* 1872, Bd. clvi. p. 36. Dragendorff was able to get ·7 or ·8 grm. of bile acid from 100 litres of urine. (*Zeitschrift f. anal. Chem.* 1872, Bd. xi. p. 467.)

[‖] F. A. Wolff, *Zur Pathologie des Ikterus*, Diss. Inaug. Königsberg, 1869. Abstract in Henle and Meissner's *Bericht f.* 1869, p. 196.

[¶] Golowin, *Arch. f. path. Anat.* 1871, Bd. liii, p. 433.

[**] H. Huppert, *Arch. d. Heilk.* 1864, Bd. v. p. 255.

[††] Pye-Smith, *Trans. of Path. Soc. of Lond.* 1873, Vol. xxiv. p. 251. He does not, however, give the method followed.

[§§] Frerichs, *op. cit.* Bd. i. p. 102, note. Ernst Bischoff, *Zeitschrift f. rat. Med.* 1864, 3te Reihe, Bd. xxi. p. 146. Kühne, *Arch. f. path. Anat.* 1858, Bd. xiv. p. 322. I attribute no value to the finding of taurin in the urine by Raczieiewsky, (Leyden, *Beiträge zur Path. des Icterus*, Berlin, 1866, p. 33), as the microscope only was used and no chemical test.

Krusenstern sought in the urine for cholestearin in four cases of jaundice as well as in other disorders; but found none.[*]

The amount of urea excreted in jaundice has of late years been much studied, especially in Paris. For it would seem likely if Meissner's theory of the formation of urea in the liver be true, that the amount of urea in jaundice would be decreased; and on these grounds: if albuminous substances be split up in the liver into glycogen, bile acids and urea, then, if the formation of glycogen cease in jaundice, the formation of urea should cease likewise. I have shown that within a few hours after the ligature of the bile ducts glycogen ceases to be found in the liver[†] and this statement has been confirmed by von Wittich.[‡] If then in jaundice no glycogen is formed by the liver, it would seem likely that the urea and bile acids would likewise cease to be made. Now Golowin certainly seems to think that in long-continued jaundice, the bile acids no longer appear in the urine;[§] and the fluid found in the dilated gall ducts after death often gives no reaction with Pettenkofer's test. But these are all cases in which the jaundice has been long continued, and it is denied by none that early in jaundice, bile acids may readily be found in the urine and in the biliary passages. So that notwithstanding Golowin's statement it would seem likely that in jaundice, at all events early in the disease, the bile acids continue to be formed. As to the urea, much doubt formerly existed whether the amount were usually low or natural. Becquerel analysed the urine of three jaundiced patients. In the first, a man, he found

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[*] Krusenstern, *Arch. f. path. Anat.* 1875, Bd. lxv. p. 415.

[†] Wickham Legg, *St. Bartholomew's Hospital Reports*, 1873, Vol. ix. p. 161.

[‡] Von Wittich, *Centralblatt f. d. med. Wiss.* 1875, p. 291.

[§] Golowin, *Arch. f. path. Anat.* 1871, Bd. liii. p. 433:

17·923 grm. was excreted in the 24. hours; in the second, a man jaundiced after a violent dispute, he found only 4·037 grm. and in a third, a pregnant woman, markedly jaundiced, 7·933 grm.[*]

A. Vogel found in a case of cancer of the liver with jaundice that the urea varied from 6·75 to 9·5 grm, a very low amount.[†] Kölliker and Müller found in a woman aged 25 with simple jaundice that the mean of urea during the jaundice was 20 grm., during convalesence 19 grm., and when in health 26 grm.[‡] Leyden, on the other hand, has recorded a case in which the urea once rose to 50 grm. in the 24 hours; three times it is noted between 30 and 46 grm. and it never fell below 23 grm.[§] There seems to have been in this case some relation between the amount of water excreted and the urea; the highest readings of urea corresponding to the highest readings of water and *vice versâ*. Bouchardat has recorded an extraordinary case in which the readings of the urea were enormously high. A man with simple jaundice, following a sudden great joy, passed 3750. C. C. of urine in the twenty-four hours: the specific gravity was 1031. The amount of solid matter passed was 220·87 grm: the urea 133·6 grm. The jaundice next day was less, and the urea only 89·18 grm. On the third day the jaundice was still less and the urea only 46·94 grm.[||] The same observer has recorded another instance of uncomplicated jaundice in which the urea ruled high, 57·2 grm. in the 24 hours.[¶]

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[*] Becquerel, *Séméiotique des Urines*, Paris, 1841, pp. 413, and 393. There is an old analysis of Braconnot in which he says he found more urea and less phosphate of lime than usual. (*Journal de chimie méd.* 1827, t. iii. p. 480.)

[†] A. Vogel, *Zeitschrift f. rat. Med.* 1854, Bd. iv. (neue Folge) p. 391.

[‡] Kölliker and Müller, *Verhandlungen d. phys. med. Gesellschaft in Würzburg*, 1856, Bd. vi. p. 497.

[§] Leyden, *Beiträge zur Path. d. Icterus*, Berlin, 1866, p. 205.

[||] Bouchardat, *Annuaire de Thèrapeutique*, 1846, p. 328.

[¶] Idem, *ibid.* 1869, p. 237.

Genevoix has published 7 cases of simple jaundice in which during the height of the jaundice the urea was markedly increased, falling to the natural standard as the jaundice disappeared. In three of these cases the urea was over 60 grm. in the 24 hours; in two, 55 grm. and in the remaining two, 45 grm. When convalescence was established, the amount fell to 23 or 24 grm. There was no rise of temperature.[*] Reuflet records another case of simple jaundice in which the attack followed violent anger, and on the third day of the disease the amount of urea was 41 grammes in 1800 C.C. of urine. The amount of urea ruled high until the jaundice began to disappear, when it sank to 27 and 26 grammes in the 24 hours. Reuflet founds a theory on this observation, and those of Bouchardat and Brouardel. He thinks that if there be no injury to the liver cells, but an increase of the circulation in the liver, a state which he assumes in simple jaundice, then the amount of urea is much increased; but if the liver cells be injured, or the circulation become slow, then the urea is diminished.[†]

Brouardel has analysed the urine of three cases of simple jaundice, and found no increase or decrease of urea. His figures vary from 26 grm. to 32·8 grm. daily.[‡] Julius Jacobs has estimated the urea in three cases: in one, complete obstruction of the ducts from a mass of cancer was present, and the amount of urea was on an average of 7 days, 56·525 grm. in the 24 hours. In two other cases it was 28·249 grm. and 27·527 grm. on an average.[§] Dr. A. W. Foot found no decrease of the amount in one of his cases.[*] Nor did Dr. George Harley in a case of jaundice lasting 18 months find any decrease until a fortnight before the death of the patient.[†]

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[*] Genevoix, *Essai sur les variations de l'urée et l'acide urique dans les maladies du foie*, Paris, 1876, p. 63.

[†] Reuflet, *Contribution à l'étude du role du foie dans la production de l'urée*, Thèse de Paris, 1879. pp. 33 and 54.

[‡] Brouardel, *Archives de Physiologie*, 1876, p. 416.

[§] Julius Jacobs, *Arch. f. path. Anat.* 1877, Bd. lxix. p. 487.

In three cases of supposed cirrhosis complicated with jaundice, Valmont found the average of the urea to be in one, 18 grammes, in the second, 15 grammes, in the third, 7 grammes. In a fourth case of jaundice supposed to be due to cancer of the liver, the mean was 13 grammes.[‡] Vulpian found in a case of cirrhosis with jaundice, that the mean was 26·849 grm.[§]

In three cases of jaundice with clay-coloured stools, J. C. Lehmann found the amount of urea decreased during the obstruction to the gall ducts, while it became greater as soon as the obstruction was removed. In the third case, the amount of urea was increased.[‖] Lehmann explains the diminution by supposing an imperfect digestion of the albuminous matters, probably because the parapeptones are not thrown down. What, however, would be the explanation of the cases in which the urea is increased in amount?

I have made observations upon the urea in ten cases of jaundice. The two cases in which the largest amount of urea was passed were likewise those in which the largest amount of water was passed, and in which the jaundice had been longest and most intense. The mean of the urea in these two cases was 28·387 and

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[*] A. W. Foot, *Dublin Journal of Medical Science*, 1876, Vol. lxi. p. 478. The amount excreted was 439·087 grains.

[†] George Harley, *Jaundice, its pathology and treatment*, London, 1863, p. 74 *et seqq.*

[‡] Valmont, *Étude sur les causes des variations de l'urée dans quelques maladies du foie*, Thèse de Paris, 1879. This thesis has been put together with much diligence, and contains a long series of analyses of the urine, chiefly in cases of cirrhosis. The estimations of the urea were made by the hypobromite process.

[§] Vulpian, *Clinique méd.* Paris, 1879. p. 272.

[‖] J. C. Lehmann, *Ugeskr. for Läger*, 1868, 3 R. vi. No. 24-26. Abstract in Virchow's *Jahresb. f.* 1868, Bd. ii. p. 143.

29·574 grm. The lowest amount of urea was met with in a case of somewhat uncertain diagnosis, in which the jaundice had lasted about two months and the stools were of a light brown; the mean of five consecutive observations was 15·975 grm. In two other cases of jaundice from cancer of the pancreas and liver, the mean amount of six observations was 18 grm. In the remaining five cases, the means varied from 19·8 to 27·28 grm.*

Upon a review of these cases it seemed to me that the amount of urea was the greatest in those patients whose general health was the best, or who were allowed the most generous diet. I do not think there is any proof that obstruction of the gall ducts causes a lessened excretion of urea; although the earlier recorded cases may at first seem to encourage such a belief. Some of the estimations of the urea lately undertaken by the French observers, apparently at the suggestion of Charcot, seem to destroy such a notion. It is, however, a hard matter on any theory to explain the great increase of urea which Bouchardat noted in his cases, and it only remains to remark that according to present observations the urea in jaundice may be low, natural, or greatly in excess; and that the laws which govern the amount of the urea in the urine of jaundice are yet quite unknown.

Baumstark found in the urine of jaundice a homologue of ordinary urea, which he looks upon as the diamide of sarcolactic acid, or the urea of sarcolactic acid. This body is also present in normal urine, but in small quantity.†

There are not many observations on the amount of uric acid daily excreted in jaundice. Becquerel found, in one of three cases, the uric acid in excess, as much as 1·153 grm. in quantity,[*] but in the remaining two it was natural. Kühne seems to think that it is always much increased,[†] and on the other hand, Ernst Bischoff, whose observations lay claim to far greater accuracy than those of Kühne, found the uric acid not increased.[‡] He explains Kühne's statement by saying, that when jaundiced urine is acidulated with hydrochloric acid, an amazing quantity of crystals is thrown down. If these crystals be collected on a filter, they dissolve when well washed with water, and the water gives an intense reaction with nitric acid; so that it is highly probable that the crystals are mostly made up of bile pigment. Dr. A. W. Foot has, however, in one case found an increase of the uric acid, the amount being 27·13 grains.[§] Dr. George Harley found ·511 and ·266 grm., and lastly none, in three analyses made one after another in a case of permanent obstruction.[||] In these two last cases the uric acid seemed to diminish or increase *pari passu* with the urea. The like was noticed by Genevoix who found that the uric acid was increased in 7 cases of simple jaundice with the urea, and that as the jaundice diminished the urea and uric acid decreased likewise.[¶] Julius Jacobs did not find the uric acid diminish or increase with the urea: his lowest reading is ·997 grm. while the urea is 56·525 grm., while in the two other cases the uric acid is 1·0038 and 1·466 to 28·249 and 27·527 of urea.[**] In Valmont's four cases, three of cirrhosis and one of cancer, the uric acid was, if anything, below the bounds of health; but in many analyses it rose and fell with the urea.[*]

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* Wickham Legg, *Med. Chir. Trans.* 1876, Vol. lix. p. 149.

† Baumstark, *Berichte d. deutschen chemischen Gesellschaft zu Berlin*, 1873, Bd. vi. p. 1378.

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[*] Becquerel, *Séméiotique des Urines*, Paris, 1841, pp. 393 and 413.

[†] Kühne, *Arch. f. path. Anat.* 1858, Bd. xiv. p. 320.

[‡] Ernst Bischoff, *Zeitschr. f. rat. Med.* 1864, Bd. xxi. p. 151.

[§] A. W. Foot, *loc. cit.*

[||] George Harley, *loc. cit.* and: "In non-malignant hepatic disease, especially towards its latter stages, the uric acid is found to be remarkably diminished." (*Urine and its derangements*, 1872, London, p. 71.)

[¶] Genevoix, *loc. cit.*

[**] Julius Jacobs, *Arch. f. path. Anat.* 1877, Bd. lxix. p. 487.

Kühne stated, in the midst of his essay on jaundice, that no hippuric acid could be found in the urine of jaundiced men; and that after benzoic acid, or its soda salts, had been given to jaundiced patients, no hippuric acid appeared in the urine, but only unchanged benzoic acid.[†] It is well known that if benzoic acid be given to men in health, an equivalent quantity of hippuric acid appears in the urine. Several observers have repeated Kühne's experiments, but all with a negative result.[‡] The source of error in Kühne's work seems to be that the urine was not examined while quite fresh, and that the hippuric acid was changed again into benzoic. The hippuric acid may in all cases be found in jaundiced urine, if looked for soon after the urine have been voided, and by the method recommended by Schultzen.

Less attention has been paid to the chlorides than to the uric acid. A. Vogel found them in his case greatly decreased. They were only ·16 to ·3 grm. in the twenty-four hours.[§] In 9 cases of jaundice in which I estimated the chlorides, I found a tolerably close relation to the urea, the chlorides being equal to about one half of the urea in 6 out of the 9. In 2 of these 3 cases the chlorides were decreased; they were both cases of cancer of the pancreas; the chlorides were about 6 grm. to 18 and 22 grm. of urea. In the remaining case, of doubtful diagnosis, of which I have spoken before while treating of urea, the chlorides were estimated on five following days. The first day the urea was 18 grm. to 21 grm. of chlorides, the second day it fell to 17 grm. of urea to 14 grm. of chlorides, and maintained this proportion through the rest of the observations.[*] I think the first day's very high reading may be caused by some error; or perhaps accidental admixture, seeing the abundance of chloride of sodium in the world.

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[*] Valmont, *Étude sur les causes des variations de l'urée, etc.* Thèse de Paris, 1879.

[†] Kühne, *Arch. f. path. Anat.* 1858, Bd. xiv. p. 319.

[‡] Folwarczny, *Zeitschr. d. k.k. Gesellschaft d. Aerzte zu Wien*, 1859, p. 225.

Schultzen, *Arch. f. Anat. Phys. &c.* 1863, p. 204.

Neukomm, Frerichs' *Klinik d. Leberkrankheiten*, Bd. ii. p. 537.

Huppert, *Arch. d. Heilkunde*, 1865, p. 93.

Horace Chase, *Arch. f. Anat. Phys. &c.* 1865, p. 392. In two of Chase's cases, however, (dogs in whom the bile ducts had been tied) he could not find hippuric acid after the benzoate of soda had been given by the mouth.

[§] A. Vogel, *loc. cit.*

Julius Jacobs in his three cases found an increase in the chlorides in nearly all: 10·717 grm. in the first, 17·818 in the second, and 14·366 in the third.[†] In Valmont's three cases of cirrhosis with jaundice, the amount of chlorides was always small; sometimes only two grammes in the 24 hours being passed.[‡]

There are also few observations upon the amount of sulphates excreted in jaundice. Kölliker and Müller found in an artificially jaundiced dog that more sulphuric acid was excreted than in a sound dog; a fact which seems to them to show that the sulphur of the taurocholic acid passes into the urine. In a case of simple jaundice in a woman, aged 25, they found, however, the sulphuric acid, as well as the urea, diminished.[§] It seems doubtful, however, if the decrease of the sulphuric acid be not due to the general state of the patient. Julius Vogel gives as evidence of the state of chronic disease, that in a jaundiced man the amount of sulphuric acid excreted in the 24 hours was only 1·4 grm.[‖] Ernst Bischoff likewise found the amount of the sulphates diminished, clearly he thinks, owing to the decreased diet.[*] But he also noticed another more interesting fact. It is well known, from Voit's observations, that the sulphuric acid in the urine does not account for all the sulphur, and that a body containing sulphur is present, probably derived from taurin. Now the amount of sulphur, not oxydised, present in the urine of jaundice is much in excess of what is natural; and the amount of excess is exactly equal to the amount of sulphur in the fæces which Bischoff calculates should be passed during health. So that Bischoff is inclined to think that the same amount of taurin, and therefore of taurocholic acid, is secreted by the liver in jaundice as in health.

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[*] Wickham Legg, *Med. Chir. Trans.* 1876, Vol. lix. p. 149.

[†] Julius Jacobs, *Arch. f. path. Anat.* 1877, Bd. lxix. p. 487.

[‡] Valmont, *Étude sur les causes des variations de l'urée*, Thèse de Paris, 1879.

[§] Kölliker and Müller, *Verhandlungen d. phys.-med. Gesellschaft in Würzburg*, 1856, Bd. vi. p. 492.

[‖] Neubauer and Vogel, *Anleitung zur qual. u. quant. Analyse des Harns*, Wiesbaden, 1863, p. 327.

I have been able to find only a few observations upon the amount of phosphates excreted: von Haxthausen notes that a jaundiced man, 36 years of age, excreted as a mean of 24 observations, 1·93 grm. of phosphoric acid in the 24 hours; the lowest being 1·364 grm.; the highest, 3·508 grm. The excretion of phosphates appears to be less before noon than afternoon, and more in the night than during the day.[†] Dr. A. W. Foot found as a result of one observation upon a jaundiced woman, that the amount of phosphoric acid excreted was 58·625 grains in the 24 hours.[‡] Julius Jacobs in one case found 1·183 grm. in the 24 hours.[§]

Except in cases of acute yellow atrophy, leucin and tyrosin are not present in the urine of ordinary jaundice. Great caution should be used in asserting that they are present in the urine in any case. The mere finding of a sediment in the urine which shows under the microscope crystals like those of leucin and tyrosin is no proof whatever that these bodies exist in the urine.* Chemical tests must be applied to the bodies crystallised out from the urine, otherwise no reliance can be placed upon the statement that they are present.

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[*] Ernst Bischoff, *op. cit.* p. 150.

[†] Von Haxthausen, Schmidt's *Jahrbb.* 1863, Bd. cxx. p. 160. Braconnot (*Journal de Chemie méd.* 1827, t. iii. p. 480.) says he once found the phosphate of lime decreased.

[‡] A. W. Foot, *loc. cit.*

[§] Julius Jacobs, *Arch. f. path. Anat.* 1877, Bd. lxix. p. 487.

Budd† Murchison‡ and Pouzol§ have noticed the occasional presence of casts of the renal tubes in jaundiced urine. Nothnagel looks upon their presence as a constant phænomenon in all cases of intense jaundice, whatever the cause may be. He thinks casts in the urine are more often present than itching of the skin; they are usually hyaline and are then not coloured yellow; epithelial casts are the next commonest, and are deeply yellow coloured; very rare are the so-called fibrinous casts. In two-thirds of the cases albumen was not found by the ordinary tests, nor any of its modifications. The cases observed were catarrhal jaundice, jaundice from gall stones, compression of duct by new growth, pyæmia, and "bilious" pneumonia.‖ Dr. Finlayson, in some observations upon the presence of casts in urine not containing albumen, says that tube casts are almost invariably found in marked cases of jaundice, and this as a rule occurs without albuminuria,¶ so that this observer agrees with Nothnagel. In the many cases in which I have carefully looked for casts, I have not been able once to find these bodies. Dr. Finlayson appears to attribute the presence of casts in the urine to the irritation caused by the passage of pigment.

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* A friend of mine, the late Dr. C. E. Squarey, well known for his experience in the analysis of the urine, was able to get abundant evidence with the microscope of the presence of leucin and tyrosin in nearly all cases of jaundice. Pushing his results further, he got the same shaped crystals in all kinds of urine, diseased and healthy, but he was in no case able to produce any evidence of the presence of these bodies in the urine of jaundice, or of any other disease when using chemical tests.

† Budd, *On Diseases of the Liver*, London, 1857, 3rd ed. p. 288.

‡ Murchison, *Clinical Lectures on Diseases of the Liver*, Lond. 1868, p. 287.

§ Pouzol, *Essai sur l'ictère*, Paris, 1872, p. 18.

‖ Nothnagel, *Deutsch. Arch. f. klin. Med.* 1874, Bd. xii. p. 326.

¶ Finlayson, *British and Foreign Med. Chir. Rev.* 1876, Vol. lvii. p. 184.

Kussmaul noted in a case of jaundice, supposed to arise from gall stones, crystals of bile pigment within epithelial cells found in the urine. The epithelium was supposed to be shed from the bladder.*

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* Kussmaul, *Würzburger med. Zeitschrift*, 1863, Bd. iv. p. 63.

CHAPTER XII.

THE COMPLICATIONS OF JAUNDICE.

Wasting. One long-noticed complication of jaundice is the wasting and weakness.[*] Even in cases of simple jaundice these symptoms are early observed. Still cases are sometimes seen in which there is scarcely any loss of flesh, and in which the patient feels no weakness even when the disease has lasted a long time. The number of persons with jaundice, seen in places of public resort, shows that in some cases it cannot be attended with any grave inconvenience.

The stoppage of the flow of bile into the intestines is followed by different results according to different observers. Some state that no harm ensues, provided that a free escape of the bile outside of the body be allowed. Others assert that bile is necessary to the digestion, especially of fats, and that if the course of the bile be diverted, death from inanition will sooner or later take place. Be the real state of affairs as it may, it is of importance to note that the glycogenetic function of the liver is abolished within a few hours after the bile ducts are obstructed.[†] This affords a clue to the wasting and debility which accompany jaundice. The value of glycogen in all processes of growth has long been known, and without the presence of glycogen it is probable that nutrition is seriously interfered with.

Temperature. The temperature in jaundice is commonly natural, or even below the standard of health. Obstruction to the passage of the bile into the intestine seems of itself to cause no rise of temperature in the body. It is otherwise, of course, if, as a cause of the jaundice, there be a febrile disease, such as pyæmia or abscess of the liver.

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[*] Hippocrates, *de morbis*, Lib. ii. Cap. xxxix. Littré's ed. t. vii. p. 54.

[†] J. Wickham Legg, *St. Bartholomew's Hospital Reports*, 1873, Vol. ix. p. 161, and v. Wittich, *Centralbl. f. d. med. Wiss.* 1875. p. 291.

Röhrig has shown that after the injection of bile acids into an animal, the temperature becomes greatly lowered,* and it is to the circulation of these in the blood that he attributes the low temperature. It seems to me more reasonable to attribute the symptom to the ceasing of chemical changes in the liver itself. The temperature of the liver is very high, higher than that of any gland in the body, the liver itself being the chief source of animal heat; if the various processes which cause this high temperature come to an end there would be at once a sufficient cause for the general temperature of the body being lowered.

It is worthy of note that if a disease commonly attended with a high temperature, such as pneumonia, for example, be complicated by a jaundice, the temperature no longer shows the usual high reading. Sometimes the temperature shows indeed no rise, even when the disease should be, from its kind, of a markedly febrile character.

Towards the end of a chronic jaundice a sudden rise in temperature may be observed, to as high as 105° or 106° F.† This rise in temperature is always of immediate bad augury,‡ and is often attended with nervous symptoms, such as delirium or coma, and too often the death of the patient follows in a few hours.

The same rise of temperature is seen in *icterus gravis* just before death, and it may very likely be only part of that rise of temperature in the agony which De Haen observed, more than a hundred years ago, in disorders not attended with jaundice.*

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* A. Röhrig, *Arch. d. Heilkunde*, 1863, Bd. iv. pp. 392, *et seqq.*

† Gee, *St. Bartholomew's Hospital Reports*, 1869, Vol. v. p. 108. Cf. the case of Charles Kingsley given in full under the head of xanthelasma.

‡ Wunderlich, *Das Verhalten der Eigenwärme in Krankheiten*, Leipzig, 1870, 2te Auflage, p. 404.

Itching. A general itching of the skin is common in jaundice,† according to Frerichs, in about a fifth of the cases,‡ although I feel disposed to rate the proportion much higher. I have of late inquired of all patients who were jaundiced, whether they had suffered from itching during the time that they were yellow, or immediately before; and I find that out of 48 cases, mostly grown-up men and women, that itching, either general or local, had been felt in 33; that is, a proportion of over 68 *per cent.*

The itching is usually worse at night, sometimes being so severe that the patients tear the skin with their nails, and papules, pustules, and even ulcerations, eczema, or nettle-rash, follow. The sensation of itching is usually spread all over the body, not confined to one particular part, though sometimes it seems to attack the trunk only. It is most severe at night.

The itching is often most intense at the outset of the jaundice, and ceases when the disease has lasted a few days. I have seen, however, the itching in some cases persist through the whole course of the disease, and cause the greatest misery to the patient, destroying sleep.

Graves mentions a case in which the itching of the skin preceded the jaundice by 10 days, and disappeared as soon as the jaundice declared itself.§

He speaks also of a case very like this in the disappearance of the itching when the jaundice set in; but the itching had persisted for two months before the jaundice came on. It is quite possible that the two cases may be nothing more than coincidences. Graves thinks that they effectually disprove the current opinion that the itching depends upon the presence of bile in the skin. Dr. Austin Flint describes a case, also in an Irishman, where the itching came on about two months before the jaundice, and was accompanied apparently by urticaria.[*] In one of my own cases, a girl of 14, the itching come on six weeks before the yellowness was observed.

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* Anton. de Haen, *Rat. Med.* Vindobonæ, 1759, Pars iv. Caput vi. p. 211.

† Hippocrates had already noticed this symptom. (*De morbis internis,* Cap. xxxvi. Littré's edition, t. vii. p. 256.)

‡ Frerichs, *op. cit.* Bd. i. p. 113.

§ Graves, *Clinical Lectures on the Practice of Medicine,* Dublin, 1864, second edition, edited by Neligan, p. 637.

That the itching of jaundice is sometimes attended by nettle-rash was noticed by Joseph Frank.[†] Graves speaks of cases of jaundice preceded by inflammation of the joints, in which he was able to foretell the appearance of the urticaria. He looks upon this sequence as invariable: inflammation of the joints, jaundice, urticaria.[‡] In a case noticed by Horaczek, the urticaria, with dyspeptic symptoms, seems to have slightly preceded the jaundice.[§]

It is not known to what cause this itching of the skin is due. As already mentioned, it is thought by some to be owing to the presence of the elements of the bile in the blood. Leyden thinks it caused, not by the inert bile pigment, but by the acids; the fluids of the tissues containing a certain amount of these, cause an irritation of the ends of the sensory nerves in the skin, and thus cause the itching felt by the patients.[||] If this theory be true, it would be interesting to know if the urine contain, at the beginning of an attack of jaundice, a larger amount of the bile acids than later on in the disease.

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[*] Austin Flint, *Philadelph. Med. Times*, 1878, Vol. viii. p. 507.

[†] Joseph Frank, *Prax. med. univ. præc.* Lipsiæ, 1843, Pars iii. Vol. ii. Sect. ii. Fascic. i. p. 279. Cf. Bamberger, *Khten. d. chyl. Systems*, Erlang. 1864, 2te Aufl. p. 472.

[‡] Graves, *op. cit.* p. 339.

[§] Horaczek, *Die gallige Dyscrasie*, Wien, 1843, p. 141.

[||] Leyden, *Beiträge zur Pathologie des Icterus*, Berlin, 1866, p. 106.

Henle suggests on the other hand that the itching may be caused by some fatty change in the secretion of the skin or by a more abundant desquamation of the epidermis.[*]

Budd looks upon itching as one of the aids to a diagnosis between jaundice from suppression and obstruction, as itching is common in the latter, not in the former.[†] The same idea is supported by Gubler, who makes the like distinction between his *ictère biliphéique* and *ictére hémaphéique*.[‡]

Dr. Murchison says that boils and carbuncles are seen in some cases of jaundice.[§] Frerichs speaks of a case in which the skin was covered with ring-shaped patches like urticaria. They did not however cause any inconvenience, and disappeared eight days after they were first noticed.[||] They could not thus have been xanthelasma.

Slow Pulse. It has been known for many years past that jaundice is often accompanied by a slow pulse, if the patient be free from fever. I am not able to say precisely who was the first to speak of this symptom. Galen describes the pulse in jaundice as smaller, harder, firmer, not weak, nor quick.[¶] The slow pulse is spoken of shortly by Corp ;[**] John Andrée certainly describes it and a case in which Dr. Hunter found it as low as 37.[††] Portal likewise mentions the symptom.[‡‡] It is only, however, of late years that an attempt to explain this phænomenon has been made. Röhrig first, in 1863, found that the injection of the bile acids into the circulation, not of pigment nor of cholestearin, was followed by a slow pulse. He went further and formed an opinion that the slow pulse was due to the action of the bile acids upon the ganglia of the heart, because the pulse became slow even if the *vagi* were cut and because the heart of the frog when immersed in serum and bile acids beat more slowly than when immersed in serum only.[*] These reasons would not now be accepted by physiologists as conclusive.

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[*] Henle, *Handb. d. rat. Path.* Braunschweig, 1847, Bd. ii. p. 205.

[†] Budd, *op. cit.* p. 287.

[‡] Gubler, in Laborde, *Phys. path. de l'ictère*, Thèse de Paris, 1869, p. 91.

[§] Murchison, *Clinical Lectures on Diseases of the Liver*, London, 1868, p. 291.

[||] Frerichs, *op. cit.* Bd. i. p. 114.

[¶] Galen, *de pulsibus*, Lipsiæ, 1824, Kühn's ed. Vol. viii. p. 491.

[**] Corp, *An Essay on the Jaundice*, Bath, 1785, p. 14.

[††] John Andrée, *Considerations on Bilious Diseases*, Hertford, 1788, p. 39, note.

[‡‡] Portal, *Obs. sur la nature et le traitement des maladies du foie*, Paris, 1813, p. 134. It will be thus seen that Pouzol (*Essai sur l'ictère*, Paris, 1872, p. 74.) was quite wrong when he said that Bouillaud (*Traité de Nosographie méd.* Paris, 1846, t. iii. p. 303.) was the first to notice the slow pulse.

Traube in the following year published an explanation upon altogether different grounds. This is based upon the well-known fact that the bile acids rapidly dissolve the red corpuscles of the blood. The bile acids, therefore, when injected into the jugular vein, destroy a large number of the red corpusles and render that part of the blood unable properly to exchange oxygen. This damaged part of the blood is rapidly sent through the lungs and brought to the left side of the heart, and thence carried into the coronary arteries of the heart. The muscular walls, being thus fed with blood quite unfit for their nourishment, become unable to contract, and a slow pulse follows. This theory accounts for the rapid disappearance of the slow pulse when once the injection has been ended.[†] Johannes Ranke likewise has expressed his belief in the muscular origin of the slow pulse. He found that when the bile acids were injected into the aorta of frogs, the muscles became hard and rigid, and did not answer to the electrical stimulus. From this he concludes that the striped muscles alone are concerned in the slow pulse of jaundice.[‡]

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[*] Röhrig, *Arch. f. Heilkunde*, 1863, p. 385. Also in an Inaugural Dissertation, *Ueber den Einfluss der Galle auf die Herzthätigkeit*, Leipzig, 1863.

[†] Traube, *Berliner klin. Wochenschrift*, 1864, p. 86; also in *Gesammelte Beiträge*, Berlin, 1871, Bd. i. p. 366.

[‡] Johannes Ranke, *Arch. f. Anat. u. Phys.* 1864, p. 340: also in *Tetanus*, Leipzig, 1865, p. 395.

I have published quite a different explanation of the slow pulse.* Johannes Ranke's theory must, I think, be rejected. It is quite true that the bile acids do cause the muscles to become hard and not to answer to the electrical stimulus, but this is due rather to a chemical than a physiological action. The bile acids, even in weak solution, coagulate albumen, and if they be injected immediately into the muscles, it is not surprising that these should become hard from the coagulation of the myosin, and lose all physiological properties. If, however, the bile acids be injected under the skin so that they may act on the muscles by a natural process of absorption, no change is seen in their powers of contraction. The curves traced by the myograph remain natural, no matter how large the dose of bile acids. On these grounds it will be impossible to attribute the slow pulse in jaundice to the failure of the muscular walls of the heart alone. Traube's theory, likewise, however ingenious, wants a basis of fact and must be rejected.

Nor is the pulse due to an excitement of the inhibitory function of the *vagus:* for if this be removed by a small dose of atropin, the slow pulse still arises when the bile acids are introduced into the circulation.

There remains, therefore, only one other factor in the movements of the heart, the ganglia; and if it be safe to argue in this case, *per viam exclusionis*, these should be the means by which the slow pulse of jaundice is caused. When the ganglia are separated from the ventricles by a ligature, no change follows in the alternate rest and action of the ventricle when the bile acids are introduced into it.†

The slow pulse is by no means common in jaundice;

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* Wickham Legg, *Proceedings of the Royal Society*, 1876, Vol. xxiv. p. 442.

† For a fuller account, see the chapter on the physiological action of the bile, p. 201 of this work.

even in cases where the temperature is natural, the pulse usually preserves the natural number of beats.[*] When the pulse is lowered, it does not usually fall very much, the beats sinking to 70 or 60, rarely lower. I have indeed seen the pulse of jaundiced patients as low as 50, and once only as low as 40. Frerichs says he has seen it as low as 21 beats.[†] It is usually quite regular. It disappears, as Traube remarked,[‡] if the patient get up and walk about. The observation must therefore be made when the patient is lying down.

Frerichs likewise remarks that the slow pulse disappears if any inflammatory action set in ; and on the contrary, if during the progress of a febrile disorder jaundice appear, the pulse at once sinks to the normal, or below it.[§] I have not met with any like instance. Vulpian has seen the palpitations of aortic and mitral disease disappear altogether during an attack of simple jaundice.[‖]

The reason that the slow pulse so seldom makes its appearance in jaundice would seem to be due to the small amount of bile acid circulating in the blood. It will be shown later on that it is in no way probable that the liver secretes any large amount of bile acids in cases of obstruction to the gall ducts, and this is borne out by the fact that a slow pulse in jaundice is not very common, for any large amount of bile acids secreted by the liver and again absorbed, would undoubtedly cause a slow pulse in every case of jaundice, as well as severe accidents in other parts of the œconomy.

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[*] Henoch remarks that he has never seen a slow pulse in the jaundice of children. Even in cases absolutely free from fever, the pulse was always 100-120. He attributes this to the great irritability of the child's nervous system, and especially to his fear of the physician, which may make up for the depressing influence of the bile acids on the pulse. (*Beiträge zur Kinderheilkunde*, Berlin, 1868, p. 342.) Rehn (*Jahrb. f. Kinderheilkunde*, 1870, Bd. iii. p. 197.) noticed this slow pulse in two children, in an epidemic of simple jaundice. Dr. Hilton Fagge says that he has never seen the slow pulse out of simple jaundice. (*Guy's Hospital Reports*, 1875, Vol. xx. third series, p. 157.)

[†] Frerichs, *op. cit.* Bd. i. p. 116.

[‡] Traube, *loc. cit.*

[§] Frerichs, *loc. cit.*

[‖] Vulpian, *Leçons*, (année 1874.) Paris, p. 143. Cours recueilli par A. Paulier.

With the sphygmograph the pulse in jaundice gives a tracing which shows a very oblique up line, which rises but little, but which is a long time in coming down to the abscissa. The polychrotism is very marked.* Kleinpeter thinks there is some increase of the arterial pressure, though there are cases in which the tension is decreased.†

Gangolphe, in an interesting thesis, has pointed out that a mitral regurgitant murmur accompanies many cases of jaundice, especially those which show the phænomena of a slow pulse. In all cases the murmur was first noticed while the pulse was slow; and, as a rule, the murmur disappeared when the pulse became quicker. The murmur is usually very soft, not harsh, heard with the first sound at the apex of the heart. The murmur is only heard in the axilla when it is very loud. In some cases it is attended by a murmur at the base, and a murmur in the larger arteries. The murmur is intermittent, and does not last after the jaundice has disappeared, thus distinguishing itself from organic murmurs.

The murmur is due partly to a slight dilatation of the heart, but chiefly to a paralysis of the papillary muscles, due to the action of the biliary constituents upon the heart. Gangolphe points out that in some cases a fatty degeneration of the walls of the heart has been noticed in acute yellow atrophy, and in acute poisoning by the bile acids. He does not think that anæmia has anything to do with these murmurs.‡

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* Marey, quoted by Straus, *des Ictères chroniques*, Paris, 1878, p. 110.

† Kleinpeter and Lorain, quoted by Straus.

‡ Gangolphe, *Du bruit de souffle mitral dans l'ictère*, Thèse de Paris, 1875. For his general conclusions see p. 41.

It is worthy of note that in some of Gangolphe's cases, a murmur was sometimes developed at the base of the heart and along the great vessels, phænomena usually associated with anæmia. In jaundice the red corpuscles are often decreased in number, and the blood is in a watery, poor state: it would be hard to disbelieve that any tendency to a murmur should not thus be aggravated. It is, however, highly probable that the murmurs are caused by the circulation in the blood of the bile acids, as the murmur is found so constantly associated with a slow pulse. Other poisons which have a direct action upon the heart sometimes cause a transient murmur, for my friend and colleague Dr. Lauder Brunton informs me that he has frequently found a mitral murmur develope in dogs when they were placed under the influence of digitalis. Dr. Brunton, like Gangolphe, attributes the murmur to an imperfect action of the papillary muscles.

I have never myself seen a murmur which passed away with the disappearance of the jaundice, though I have not unfrequently seen jaundice develope in persons already the subject of heart disease.

Fabre says that since the publication of Gangolphe's thesis, he has noticed a murmur over the heart in five out of eight cases of jaundice. He attributes the murmur to a myocarditis caused by the toxic action of the bile acids.*

Potain has other views as to the cause of the murmurs heard in jaundice. He thinks that the liver will be found to hold the same connexion with heart disease that the kidney does, and that in diseases of the liver, especially in chronic jaundice, there will be enlargement of the heart, chiefly of the right side; a dilatation, rather than hypertrophy, with tricuspid incompetence, as a result of the disease of the liver; not I must own as we are now accustomed to think, that the disease of the liver, as nutmeg liver, is secondary to the tricuspid regurgitation.*

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* Fabre, *Gaz. des Hôp.* 1877, p. 916.

Changes in Power of Perception. In some cases of jaundice, the senses of taste and sight seem to suffer, and to give wrong intelligence to the patient. Neither of these phænomena is common, but it is characteristic of the love of the marvellous that upon these two symptoms, the non-medical mind should have fastened as essential.

i. *Bitterness of Taste.* It is said that patients with jaundice sometimes complain of a bitter taste; and in ancient times this was thought to be invariable.† I have myself not met with any such perversion of taste in my own cases. It has been thought to be due to the passage of bilious matters into the mouth,‡ apparently through the saliva; and the behaviour of animals, during the injection of bile acids into their veins, might be pointed out in support of this view. The creatures thrust out their tongues, and lick their lips and jaws as if to rid themselves of a disagreeable sensation.§ I should myself look upon the gastric state which accompanies so many cases of simple jaundice as a more probable cause of a bitter or disagreeable taste rather than the circulation of the bile acids in the blood, or their escape through the saliva, although Dr. Fenwick has attempted to prove that they may not uncommonly be found in the saliva of jaundice.‖ Heberden says it is far from uncommon to have all solid and liquid food taste bitter; and speaks of one to whom everything tasted bitter, except oysters.¶

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* Potain, reported by Straus, *Des Ictères Chroniques*, Paris, 1878, p. 114.

† M. A. Antoninus, *Thoughts*, vi. 57, Long's Transl. London, 1869, Sec. ed. p. 130. "To the jaundiced honey tastes bitter."

‡ Henle, *Handb. d. rat. Path.* Braunschweig, 1847, Bd. ii. p. 206.

§ See p. 192 of this work.

‖ Fenwick, *Lancet*, 1877, Vol. ii. p. 303.

¶ Heberden, *Commentaries*, Lond. 1806, 3rd ed. p. 247.

ii. *Yellow Vision.* In some rare cases of jaundice, all, or only white, objects appear yellow to the patient. The first account of this symptom on record is given by Lucretius, a non-medical writer, who says:

> "Lurida præterea fiunt quæcomque tuentur
> Arquati."[*]

words which have passed into a proverb.[†] Galen likewise speaks of the symptom, saying that all objects are seen yellow by the jaundiced.[‡]

Although this symptom is by no means common, yet Sydenham, the pride and glory of English medicine, speaks of it as part of the definition of jaundice, that all objects appear yellow.[§] Mercurialis, on the other hand, altogether rejects this appearance as unheard of.[‖] There can be no doubt, however, of its occasional appearance. I have myself, during three years, met with no less than three cases. Still many writers look upon it as a symptom of great rarity. Peter Frank says that in the course of 54 years, he met with this symptom only five times;[¶] and Frerichs says he has never seen a case although he has always asked for the symptom.[**]

Yellow vision is usually seen only in intense jaundice, and then for no great length of time, for the symptom rapidly passes off. I have, however, seen yellow vision last for three days. As a rule, only white objects appear yellow; but in some severe cases all objects have a yellow shimmer.

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[*] Lucretius, *de rerum natura*, Lib. iv. 331. Some think that Hippocrates speaks of this symptom, (*De locis in homine* Cap. 16) when, as some read, it is said that jaundice is dangerous when it falls upon the eyes. Littré (his edition of Hipp. t. vi. p. 308.) adopts quite a different construing.

[†] They are quoted by Montaigne in his long essay on natural religion or apology for Raymond of Sebonde, (*Essais*, Livre ii. Chap. xii.) to show how completely we are at the mercy of our senses. See also Sextus Empiricus, *Pyrrhon. Hypot.* Lib. i. Cap. xiv.

[‡] Galen, *De symptom. different.* Cap. ii. Kühn's ed. Vol. vii. p. 99.

[§] Sydenham, *Processus Integri*, Cap. xxix. ed. Greenhill, p. 582.

[‖] Mercurialis, *Var. Lect. in Med. Script.* Venetiis, 1598, Lib. vi. Cap. xii. p. 129.

[¶] J. P. Frank, *De curand. hom. morb. epitome*, Viennæ, 1821, Lib. vi. Pars iii. p. 307.

[**] Frerichs, *op. cit.* Bd. i. p. 115.

The cause of the yellow vision is quite unknown. Many, led by Morgagni,[*] have thought it to be due to the impregnation of the humours of the eye by bilious fluids. Peter Frank, however, objected to this doctrine on three grounds: i. that he had often seen the cornea yellow without disturbance of vision; ii. that the yellow vision is often intermitting; and iii. that a woman, suffering from typhoid, who had never been jaundiced, saw all things yellow for two days.[†]

He allows that yellow vision may sometimes arise from coloured humours or membranes of the eye, yet he evidently thinks that the whole phænomenon may well be explained on nervous grounds. Joseph Frank, following his father, points out that the disorder is not unfrequently attended by night blindness, and that it is very possibly due to some changes in the optic nerve.[‡] Stokes seems likewise to favour the view of nervous origin.[§]

Elliotson, on the other hand, made a return to the views of Morgagni. He found that one of his patients who was jaundiced, saw yellow with the left eye, and not with the right; in the left, two large red vessels ran over the cornea; in the right, there was no enlargement of the vessels. Elliotson infers that the serum of the blood passing in front of the eye tinges all things yellow. He had soon after this another jaundiced patient who saw yellow, and in whom the conjunctiva around the cornea was greatly inflamed.[‖] Sir Thomas Watson, likewise, records the case of a patient who saw yellow, and who had several varicose and singularly tortuous vessels proceeding across the sclerotica towards the cornea, and some of them reached its margin. He endorses Elliotson's view and thinks that the vessels when enlarged by disease, give a passage to the yellow colouring matter, so that all things appear as if viewed through yellow stained glass.* Dr. Murchison records a case of yellow vision, in which the conjunctival vessels were large both during and after the yellowness of sight.†

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[*] Morgagni, *De sedibus, etc.* Ep. xxxvii. Art. 8. Cf. Le Cat, *Traité de la couleur de la peau humaine*, Amsterdam, 1765, p. 161. He found in a case of jaundice the aqueous and vitreous of a yellow tint.

[†] J. P. Frank, *op. cit.* p. 344.

[‡] Joseph Frank, *op. cit.* p. 276. Bamberger (*Krankheiten d. chyl. Syst.* in Virchow's *Handbuch*, Erlangen, 1864, 2te Aufl. p. 473.) remarks that all the cases of day and night blindness, which he has seen associated with jaundice, have died.

[§] Stokes, *London Med. and Surg. Journal*, 1834, Vol. v. p. 200.

[‖] Elliotson, *Lond. Med. Gaz.* 1833, Vol. xii. p. 486.

Rose has supported Peter Frank's theory of a nervous cause for the yellow vision. In one of his cases he found a marked Daltonism, an inability to distinguish red, as well as a seeing of objects yellow. He found the humours of the eye very imperfectly coloured and dismisses these as a cause of the yellow vision.‡ Unfortunately in this case it was impossible to ascertain if the Daltonism existed in health. Santonin seems to cause a like yellow vision and a like Daltonism. The phænomena of the two may be profitably compared together.

During the last three years I have met with three cases of yellow vision in jaundice. Like Heberden's cases they have all been women.§ In one case an old woman aged 66 was examined with the ophthalmoscope. The beginnings of cataract hindered the disc of the left eye from being seen; in the right the disc was somewhat pink. Nothing else unnatural was seen. There were no enlarged vessels. The skin was intensely jaundiced, the stools colourless; the liver stretched two fingers' breadth below the margin of the ribs. Only white things were noticed to be yellow. She died shortly afterwards in her own home.

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* Thomas Watson, *Lectures on the Principles and Practice of Physic*, Lond. 1857, Vol. ii. p. 605.

† Murchison, *Clinical Lectures on Diseases of the Liver*, London, 1868, p. 295.

‡ Rose, *Arch. f. path. Anat.* 1864, Bd. xxx. p. 442. Dr. Moxon (*Lancet*, 1873, Vol. i. p. 130) examined 7 cases of jaundice in which there was no xanthopsy, and found the humours of the eye perfectly colourless.

§ Heberden, *Commentaries*, London, 1806, Third ed. p. 242.

In a short research which was conducted by Dr. Vincent Harris and myself, the power to judge of colours was tested, without beforehand asking the patient if he saw yellow. 15 patients, suffering from jaundice due to various causes, were examined on the following plan: a sheet of paper upon which were painted many of the various shades of the primary colours was presented to the patient, and he was desired to name the colours as they were pointed out. Particular attention was directed to the judging aright of blue, green, and red. In every case, save two, perfectly correct answers were given, even to minute shades of colour. One of these was an old Irishwoman, and we put little trust in what she told us. The second was a man, aged 21, with simple jaundice, who persisted in stating that green was yellow. After this they were all examined with Rose's instrument* to test their Daltonism; but with this, no change was noted. The patients were likewise examined with the ophthalmoscope with a negative result.†

Since the publication of Stilling's sheets for testing eyes, I have used them in every case of jaundice that I have met with, but I have seen no loss of power in detecting at once the various figures and letters.

Hæmorrhagic Diathesis. In some acute forms of jaundice, and in chronic jaundice which has lasted for a long time and draws towards its end, hæmorrhages from the mucous membranes and under the skin are far from uncommon.

I do not know if the short account given by Hippocrates himself of certain persons who became jaundiced during the course of a fever, but who were relieved by an abundant hæmorrhage, may be looked upon as some description of the hæmorrhagic diathesis in jaundice.[*] Huxham speaks at length of the hæmorrhagic diathesis in jaundice, saying that the hæmorrhages are not uncommon in the more severe kinds of jaundice, and that the blood comes forth from all the openings of the body, and that the bleedings yield to no remedies.[†] Richard Bright, in his valuable papers on jaundice, notices that, at the end of the disease the patient becomes drowsy, ecchymosis takes place in various parts, and blood escapes from different surfaces. In the more active and febrile forms, he says, this hæmorrhagic tendency may come on very early and be excessive.[‡] The appearance of a hæmorrhagic diathesis has likewise been noted by Budd,[§] Bamberger,[‖] Leyden,[¶] Murchison,[**] and others; it has been made the subject of an essay by Monneret[††] and Laugier,[‡‡] and numerous single cases will be found scattered through the journals.

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* For an account of this, see Rose's paper in *Arch. f. path. Anat.* 1863, Vol. xxviii. p. 35.

† Wickham Legg and Vincent Harris, *St. Bartholomew's Hospital Reports*, 1876, Vol. xii. p. 167.

The hæmorrhagic diathesis is seen very markedly in the jaundice which accompanies acute yellow atrophy of the liver. It will be fully described hereafter. In chronic jaundice the hæmorrhages rarely appear save towards the end of the patient's life; they are of a very grave, if not fatal, significance. Epistaxis is an extremely common form of hæmorrhage, and the bleeding is often very abundant. Hæmatemesis and hæmorrhage from the bowel are also very common. Hæmaturia is not nearly so common, but it has been seen[*] and also traumatic hæmorrhages, as from leech bites.[†] Petechiæ are often seen on the skin, and after death on the serous membranes. The gums and conjunctiva sometimes bleed and show petechiæ.

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[*] Hippocrates, *Epidem.* liber i. Cap. viii. Littré's ed. t. ii. p. 642. Hæmorrhages in diseases of the liver were certainly noted by Hippocrates (*Prognostic.* Cap. vii. Littré's ed. t. ii. p. 126.)

[†] Huxham, *Obs. de Aere, etc.* Londin. 1739, p. 142. The very words of Huxham are quoted by Joseph Frank (*Prax. med. univ. præc.* Lips. 1843, Pars iii. Vol. ii. Sect. ii. p. 314, note) as those of Forestus, a writer of the latter half of the seventeenth century. I have tried to verify the reference (*Obs. et cur. med. et chir. op. omnia*, Rothomagi, 1653, Lib. xix.) given by Frank, but have failed.

[‡] Bright, *Guy's Hospital Reports*, 1836, Vol. i. p. 614.

[§] Budd, *On Diseases of the Liver*, London, 1857, 3rd edit. pp. 228 and 473.

[‖] Bamberger, *Krankheiten d. chylopoëtischen Systems*, Erlangen, 1864, 2te. Auflage, p. 584.

[¶] Leyden, *Beiträge zur Path. d. Icterus*, Berlin, 1866, p. 108.

[**] Murchison, *Clinical Lectures on Diseases of the Liver*, London, 1868, p. 294.

[††] Monneret, *Arch. gén. de Med.* 1854. Vol. i. p. 641.

[‡‡] Laugier, *Des hémorrhagies liées au rétrécissement des voies biliaires*, Thèse de Paris, 1870.

The amount of blood lost may be so great as to cause death. The bleedings may begin several months before death[‡] and continue with intermissions till the patient either die of the bleedings, or of the cause of the jaundice.

Hæmorrhages have likewise been seen in the meninges of the brain and the ventricles.[§] Floodings are sometimes seen; and hæmorrhages into the ovary, into the muscles, in fact into every part of the body.

Hæmorrhages in chronic, as well as in acute jaundice are more common into the stomach and intestine than into other parts, if epistaxis be excluded. In chronic jaundice, this may be explained by the disturbance in the circulation of the liver, a theory adopted by Budd. In *icterus gravis* it is not so easy of solution.

The cause of these hæmorrhages in chronic jaundice is obscure. It is not merely the marasmus which accompanies the disorder, as the hæmorrhages are seen in acute jaundice, or the impoverished state of the blood, as Budd supposes,[||] but it seems to be the jaundice itself, that is the bile circulating in the blood, which is the source of the hæmorrhage. Of the elements of the bile, the only one known to possess any power of begetting hæmorrhages is the bile acids, and it is to the action of the bile acids upon the blood corpuscles that Leyden seems inclined to attribute the phænomena.* Were this the case, hæmaturia ought to be a constant accompaniment of the hæmorrhagic diathesis, just as it is always seen after the injection of bile acids into the circulation; a large amount of hæmoglobin being set free in the plasma of the blood and thrown out by the kidneys.

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[*] Laugier, *op. cit.* p. 11. Monneret, *loc. cit.*

[†] Laugier, *op. cit.* p. 16. Mettenheimer, *Beiträge zu der Lehre von den Greisenkrankheiten*, Leipzig, 1863, p. 120.

[‡] Laugier, *op. cit.* p. 19.

[§] Reclus, *Gaz. des Hôp.* 1872, p. 260.

[||] Budd, *op. cit.* p. 473.

It is most in accordance with the present state of knowledge to believe that hæmorrhages are preceded by a diseased state of the blood vessels, and it is to the state of blood vessels rather than to the state of the blood that hæmorrhages are due. If this be granted, it will be necessary to search for some cause of disease of the blood vessels in chronic jaundice. Leyden has shown that the bile acids cause a parenchymatous degeneration, not only of the glands, but also of the muscles.† If the middle coat of the arteries share in this degeneration, a sufficient cause of hæmorrhages is set up. It will be interesting to watch, as opportunity offers, for evidence of an extensive degeneration of the vessels in cases of hæmorrhage in jaundice, such as very probably exists in all cases of *icterus gravis*.

A curious hæmorrhagic diathesis often attended by jaundice is seen in the umbilical hæmorrhage of the new-born. Out of 220 cases which Grandidier has collected, jaundice was present in 84; in 35, jaundice and ecchymoses were seen together, and this appears to be a most serious complication, for out of the 35 only 3 recovered.‡

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* Leyden, *loc. cit.*

† Leyden, *op. cit.* p. 100.

‡ Grandidier, *Die freiwilligen Nabelblutungen der Neugeborenen*, Cassel, 1871, p. 62.

When hæmorrhages set in during the progress of a case of jaundice, the prognosis becomes very grave, but not, as Laugier asserts, altogether fatal. Monneret and other writers have recorded cases of recovery after epistaxis and even petechiæ.* There are also cases on record of recovery, even when a hæmorrhagic diathesis has set in in cases of umbilical hæmorrhage complicated with jaundice. Fränkel† has published the notes of a very interesting case. A man, aged 31, during the course of a simple jaundice was attacked by hæmatemesis and hæmorrhage from the bowel. He recovered quickly from the jaundice after hæmorrhage had ceased; the day after the hæmorrhage had stopped the urea passed in 24 hours, rose from 10 grammes to 42·17. The chlorides during the highest reading of the urea were small in amount, but rose as the urea fell. The rise in the urea after hæmorrhage is known.

Nervous Symptoms. In nearly all cases of *icterus gravis*, and in most cases of chronic jaundice just before death, delirium and coma, and sometimes convulsions, set in.‡ In some cases the appearance of the nervous symptoms is attended by a rise of temperature.

The cause of these phænomena and the various theories which labour to explain them will be best fully discussed under the head of *icterus gravis*. It may here be stated that many authors believe them to be due to a circulation of the bile elements in the blood, a cholæmia, while others attribute them to a uræmia.

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* Monneret, *Arch. gén. de Méd.* 1854, Vol. i. p. 641, and *de l'ictère hém. ess.* Paris, 1859, p. 14, from *Journal de Progrès.*

† Fränkel, *Charité-Annalen*, 1876, Bd. iii. Berlin, 1878, p. 292.

‡ Hippocrates has said: κακὸν δὲ ἐπὶ ἰκτέρῳ μώρωσις (*Praen. Coacae* vi. 194. Littré's ed. t. v. p. 626.) but in modern times Bamberger (*Krankheiten d. chyl.-poët. Systems*, Erlangen 1864, 2te Auft. p. 473.) was, I believe, the first to point out how common the nervous symptoms are at the end of chronic jaundice. My own experience is completely in accordance with that of Bamberger's. Bright (*Guy's Hosp. Reports*, 1836, Vol. i. p. 609.) says that the patient becomes drowsy in the last stage of jaundice, and that (p. 614) when the disease is more acute and febrile, the nervous symptoms come on early.

Schönlein strangely attributes the delirium to the deposit of bile pigment in the membranes of the brain.[*]

In nearly all cases of jaundice, although there may be no marked brain symptoms, as delirium, &c. yet there seems a change of humour:[†] the patients become fretful and peevish. They are disposed to sleep and indisposed to any mental exertion.

Xanthelasma. After jaundice has lasted for some months, there appear, now and then, upon the eyelids, small, oval or rounded, symmetrical patches of the colour and appearance of chamois leather, now called, by the greater number of observers, xanthelasma.[‡] Xanthelasma palpebrarum is seen in other diseases besides jaundice. Dr. Church has shown its hereditary character,[§] and Mr. Hutchinson, who has made a great study of this disorder, has pointed out its connexion with the state called by the older physicians the "bilious state;" that is, headache and vomiting; the seat of the bilious state being the stomach, not the liver. Xanthelasma has also been seen in diabetes; but there seems no good grounds for associating xanthelasma with any special morbid state save jaundice.[||]

Rayer seems to have been the first to describe and figure xanthelasma;[¶] the patient does not seem to have been jaundiced. The disease was afterwards named vitiligoidea by Addison and Gull.[*] Within the last 10 years the disease has drawn a great deal of attention both in England and in Germany, Dr. Murchison[†] and Waldeyer[‡] being the first to point out the true histological characters of the spots.

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[*] Schönlein, *Klinische Vorträge*, Berlin, 1842, p. 311.

[†] Hippocrates speaks of the great irritability of temper in the jaundiced. (*De aff. int.* cap. xxxv. Littré's ed. t. vii. p. 252.) I cannot, however, think that he referred to the delirium of jaundice in the passage where he distinguished between the effect of bile and phlegm. Those who become mad from phlegm are quiet, do not cry out and are not agitated; but those who become mad from bile cry out, are mischievous, and always in movement. (*De morbo sacro*, cap. xv. Littré's ed. t. vi. p. 389. Cf. *Democrit. epist.* t. ix. p. 385.) It seems to me that jaundice is not spoken of, but that madness is explained on the old humoral pathology.

[‡] This name was first proposed by Mr. Erasmus Wilson (*On diseases of the skin*, Lond. 6th ed. 1867, p. 773.) It is derived from ξανθός, yellow, and ἔλασμα, metal beaten out.

[§] W. S. Church, *St. Bartholomew's Hospital Reports*, 1874, Vol. x. p. 65.

[||] Hutchinson, *Med. Chir. Trans.* 1871, Vol. liv. p. 171.

[*] Rayer, *Traité des Maladies de la Peau*, Paris, 1835, 2e. éd. *Atlas*, pl. xxii. fig. 15. The young man spoken of by Portal, (*Maladies du Foie*, Paris, 1813, p. 121.)

Besides the names of xanthelasma and vitiligoidea, this appearance has been likewise called xanthoma by Frank Smith,[§] a term adopted by Kaposi.[‖] Virchow has proposed to call it *Fibroma lipomatodes*,[¶] a name which does not seem to have been followed by anyone, and against which Dr. Pye-Smith has with great justice protested.[**] *Stearrhœa flavescens* and *molluscum cholestérique* are other names which it is to be hoped will (in like manner) be soon forgotten.

Xanthelasma is not caused save by a long continuance of the jaundice. The shortest time in which I have seen it arise is six months after the first onset of the jaundice, and Dr. Pye-Smith in less than four.[‡‡] It is, however, rarely seen earlier than twelve months. It does not seem to be needful that the jaundice should be intense, but that it should be continuous; and what, in cases of jaundice, determines the xanthelasma is quite unknown. It is not dependent on the variety of jaundice, as Mr. Hutchinson thought probable,[§§] the disease being seen with a small amount of icteric

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who suffered from jaundice for three years, and was then attacked by tubercles or a sort of wart on the back and legs probably had xanthelasma.

[*] Addison and Gull, *Guy's Hospital Reports*, 1851, Series ii. Vol. vii. p. 265.

[†] Murchison, *Trans. of the Path. Soc. of London*, 1869, Vol. xx. p. 187.

[‡] Waldeyer and Jany, *Sitzbb. d. schles. Gesell. f. vaterländ. Cultur*, Juli, 1868, quoted in Virchow's *Jahresb f.* 1869, Bd. ii. p. 548.

[§] W. F. Smith, *Journal of Cutaneous Medicine*, London, 1869, Vol. iii. p. 241.

[‖] Kaposi, *Hautkrankheiten*, Stuttgart, 2te Auflage 1876, Bd. ii. p. 251. in Virchow's *Handb. d. spec. Path. und Ther.* Bd. iii. Abth. ii.

[¶] Virchow, *Arch. f. path. Anat.* 1871, Bd. lii. p. 508.

[**] Pye-Smith, *Guy's Hospital Reports*, 1877. p. 113.

[‡‡] Pye-Smith, *op. cit.* p. 127.

[§§] Hutchinson, *op. cit.* p. 181.

staining and bilious stools, as well as with the severe *melasicterus*. Nor is xanthelasma associated with any peculiar disease of the liver; any obstruction to the hepatic duct, without the liver being involved in the disease, may give rise to the skin affection, as Dr. Moxon's case shows.* I think it will prove doubtful if the xanthelasma associated with jaundice be more common amongst men than woman. Mr. Hutchinson found that xanthelasma from all causes was twice as common in women as in men.† Few, however, of his cases were jaundiced. In my own experience, I have met with six cases of jaundice associated with xanthelasma. Four of these were men; two women.

As to the age of the patient, it is generally thought that xanthelasma does not attack young persons. I have, however, met with a case of xanthelasma and jaundice in a girl aged 18 years: Kaposi, a doubtful case indeed without jaundice, in a young man, aged 24, who had patches of xanthelasma the size of wheat corns at the root of the penis,‡ and another doubtful case spoken of by Dr. Pye-Smith in a boy aged 18 associated with jaundice.§ The greatest age at which xanthelasma from jaundice seems to have been observed is Dr. Pye-Smith's case in which the xanthelasma appeared at the age of 57.‖ It is hard, however, among the poor to be sure of the age at which xanthelasma appears. Often it happens that they are quite ignorant of the existence of the patches until they are pointed out to them; and this no matter what the cause of the disorder.

Xanthelasma was divided by Addison and Gull into vitiligoidea plana, and tuberosa. The flat variety is chiefly met with on the eyelids, commonly on the inner half, and arranged with symmetry on each side. It is seen also in the face and cheeks, on the conjunctiva, and the mucous membranes of the mouth and air-tubes. It may be seen also on the prepuce and *glans penis*,* and even under the nails. They vary from a pin's point to a florin in size; Kaposi says he has seen some as large as a thaler.† They are of a pale yellow white colour, like a dead leaf, slightly raised above the surrounding skin or mucous membrane, soft, and irregular, but tending to the form of a circle. They cause no pain or inconvenience, for the patients are often not aware of their presence.

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* Moxon, *Transactions of the Pathological Society of Lond.* 1873, Vol. xxiv p. 129.

† Hutchinson, *op. cit.* p. 175.

‡ Kaposi, *op. cit.* p. 256, note.

§ Pye-Smith, *Guy's Hosp. Reports*, 1877, p. 101.

‖ Pye-Smith, *Transactions of the Path. Soc. of Lond.* 1873, Vol. xxiv. p. 250.

A variety of the plane is the linear form of xanthelasma, best seen in the palm as white lines following accurately the flexures caused by the bending of the hand and fingers. It is also seen in the soles along the flexures of the toes.

The favourite seats of the tuberose variety of xanthelasma are the ears, neck, and trunk; the back of the elbows, and hands, knuckles of the fingers; in the ham, knees, and on the feet. It is seen small as a millet seed, or of the size of a horse bean, the patches may seem much larger if individual tubercles become confluent. The skin over the tubercles is smooth, sometimes shining, and moves with them. In some cases of tuberose xanthelasma of the knuckles, the spots have been adherent to the extensor tendon underneath.

The tuberose form, unlike the plane, shows a disposition to cause annoyance to the patient. In some cases, tools could no longer be handled, walking and sitting only be accomplished with trouble. There is

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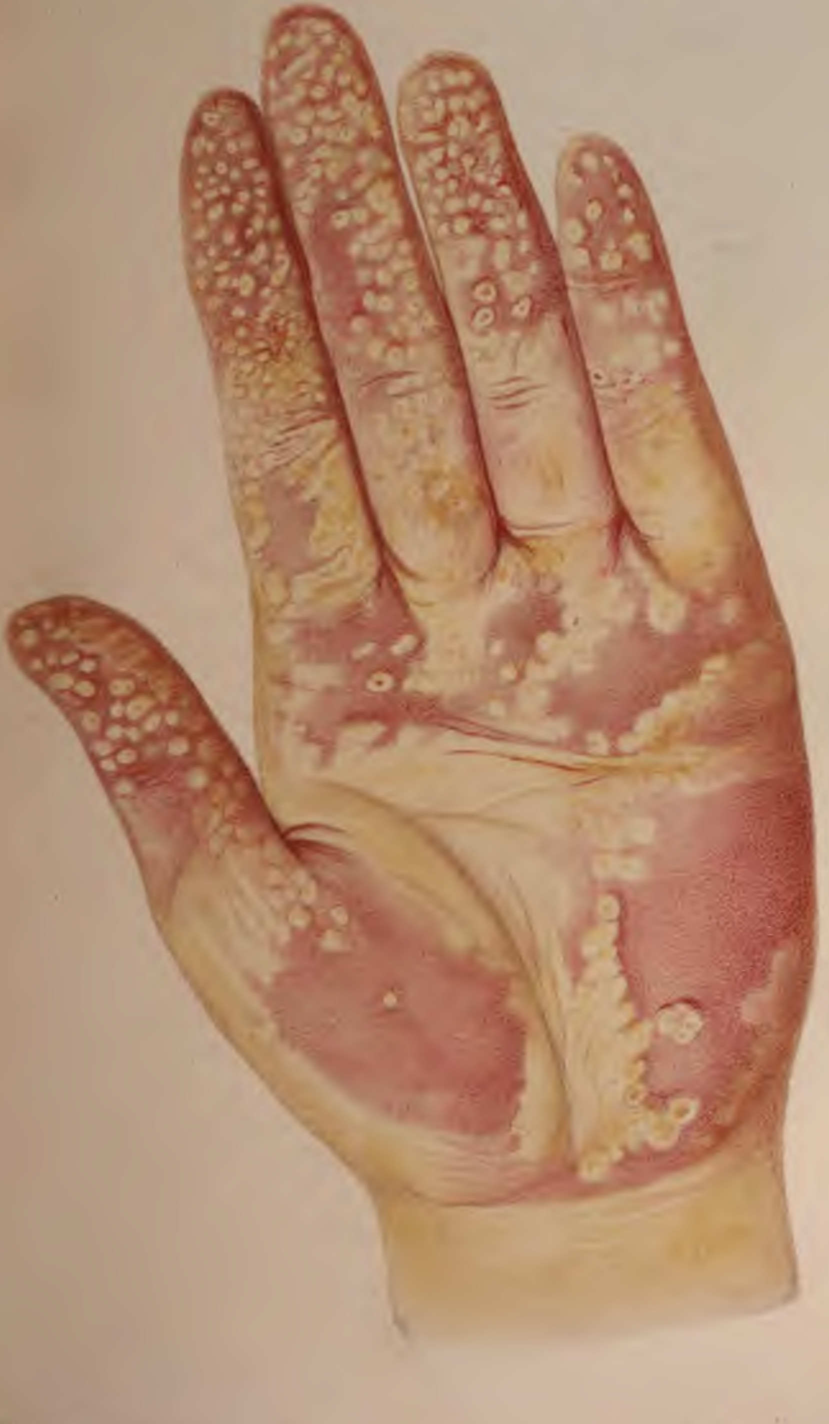
* Hillairet, *Bulletin de l'Académie de Méd.* 1878, 42me année, p. 1172.

† That is, bigger than our half-crown. Kaposi, *op. cit.* p. 253.



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XANTHELASMA OF THE HAND

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sometimes a feeling of burning and itching, though it is doubtful how much of this may be due to the presence of the jaundice. The tubercle, if cut across, bleeds profusely.

All forms of xanthelasma show a tendency to symmetry, whether appearing on the limbs or on the mucous membrane. Thus both eyelids are usually affected, both hands and elbows. In a case of my own, the mucous membrane on both sides of the tongue was seized on by xanthelasma in a markedly symmetrical manner. (See No. I. and No. II. of the chromo-lithographs, and the case of Charles Kingsley, at p. 327, of this work.)

Even when jaundice is the cause of xanthelasma, the patches would seem to first appear in the neighbourhood of the eyelids, and in many cases to spread no farther. In much rarer cases the xanthelasma appears all over the body, and is then called xanthelasma multiplex.

As to the nature of xanthelasma: Hebra seems at first to have believed that xanthelasma was due to some sebaceous obstruction, like milium or comedo.[*] Against this view, it may be urged that when a spot of xanthelasma is cut across, nothing but a bloody fluid can be pressed out, no white accumulation can be removed, and the yellow spot cannot be got rid of by pressure. This view of xanthelasma has, indeed, I think been given up by its author, and the view expressed by Dr. Pavy now prevails. He was the first to examine a nodule of xanthelasma with the microscope, and found it to be formed of a very dense fibrous tissue, pervaded with fat granules.[†]

Waldeyer was, however, the first to give a full and accurate account of the xanthelasma palpebrarum. He found that the yellow colour was due in but a very small degree to the increase of the stellate pigment cells which may naturally be found in the eyelids. These cells were met with in numbers only slightly greater than usual. They were found near the epidermis and especially about the hair follicles, vessels, and nerves, yet never so thickly set together that the yellow colour of the xanthelasma patch could be caused by it. The chief change in xanthelasma is a great multiplication of the connective tissue corpuscles in those places where naturally in the eyelid they are more numerously grouped together: therefore around the hair follicles, glands, vessels, and nerves. There follows upon this a fatty degeneration of these new-formed cells. So both these processes together explain the physical characters of xanthelasma, the formation of yellow raised patches. Thus Hebra is quite wrong, as the whole process takes place in the connective tissue of the eyelids, and not in the glands. It is thus an interstitial and not a parenchymatous process. But although xanthelasma has many points in common with dermatitis, new formations in the skin, and syphilis, yet notwithstanding it has something peculiar in itself. The fat, for example, in the new-formed cells is not so granular as in ordinary fatty degeneration, large drops are readily formed; without, however, forming ordinary fat cells. The deposition of fat likewise seems to have no harmful effect upon the cells themselves; as after the fat is taken away by reagents, the cell is always found with nucleus and protoplasm, even after the xanthelasma has lasted many years, and thus Waldeyer has never met with softening, a milky detritus, masses of cholestearin, or calcification, accidents commonly seen after fatty degeneration. Xanthelasma never seems to undergo a retrogressive metamorphosis, and this is one of its most interesting peculiarities.*

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[*] Hebra, *Atlas d. Hautkrankheiten*, Lief. 7, and *Diseases of the Skin*, Trans. by Hilton Fagge, *New Sydenham Soc.* 1866, Vol. i. p. 127.

[†] Pavy, *Guy's Hosp. Reports*, 1866, p. 282.

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* Waldeyer, *Arch. f. path. Anat.* 1871, Bd. lii. p. 318.

Leber has confirmed these observations in a case of xanthelasma multiplex reported by Virchow. In the smaller tubercles of xanthelasma, however, no fatty infiltration of the cells was to be seen; only a few cells contained a few yellow to yellow-brown pigment granules.* Still it would seem certain that the colour of xanthelasma is due to fat and not to pigment; and this is the more remarkable since jaundice is attended by a deposit of pigment in the skin. Waldeyer's account of xanthelasma palpebrarum may, I think, be safely applied to the xanthelasma of the rest of the body. I have examined patches from the tongue and the scrotum, and found very nearly the same appearances as he has. In the scrotum the cuticle was not thickened over the patches; collections of oil globules in long streaks were seen in the deeper layers of the subcutaneous connective tissue. In some cases there was, as Waldeyer has described, an accumulation of oil globules around the hair follicles, vessels, and other structures passing through the skin;. but this was not universally true. The papillæ of the skin seemed unaffected; the collection of oil drops, though somewhat bent towards the papilla as it passed under it, did not enter it. When examined with a high power, the collection of fat drops showed many cells, varying much in size. The very smallest were not so large as a red blood corpuscle, and were round, oval, rhomboidal, and spindle shaped. These small cells were free from granular contents; showing one or even two nuclei. The cells larger than these were slightly granular. Then there were cells four or six times the size of the smallest; round or oval in shape; filled with fat, and therefore no nucleus to be seen. The fat was not in many drops but in one large drop, distending the cell.

Some of these large fat-containing cells had a sinuous appearance; apparently brought about by the pressure of the fibres. The patches of the tongue showed appearances in all important respects like those of the scrotum. It is thus evident that the xanthelasma of the mucous membranes and the xanthelasma of the skin are alike in their nature. The same, however, cannot be predicated of the yellow patches seen under serous membranes in cases of multiple xanthelasma. I have examined these spots, which to the naked eye closely resemble those of xanthelasma, and find that the appearance is caused by a spindle-shaped cavity in the connective tissue under the peritonæum, filled with ordinary adipose tissue. These patches, therefore, differ altogether in nature from xanthelasma, and seem to be a mere local accumulation of fat under the peritonæum.

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* Leber, reported by Virchow, *ibid.* p. 506.

There is, undoubtedly, a superficial resemblance in the process seen in xanthelasma to that of atheroma in the arteries. The great difference between them lies, as Virchow has pointed out, in the absence of any true fatty degeneration.* Both in xanthelasma and atheroma there is a chronic process of cell growth, followed by a fatty infiltration of the cells; but in xanthelasma there is no fatty degeneration; the cells do not, as in atheroma, break up and form a fatty detritus, a change followed in time by the formation of cholestearin, by calcification, and ulceration. Xanthelasma may last for years, and yet the cells, although filled with fat, are perfectly retained, and no retrogressive changes are met with. Mr. Howse, however, has seen, in a case of Dr. Hilton Fagge's, appearances of further degenerative changes, the middle part of the patch, as in atheroma, being converted into lumps of calcareous matter and crystalline bodies.† From these appearances it was judged that xanthelasma and atheroma were identical in nature. This opinion can, however, hardly be accepted, as it is opposed to the observation of all other histologists, until many other cases of xanthelasma of the same kind have been examined, and like appearances of fatty degeneration found. The spontaneous disappearance of xanthelasma without scarring is also against the idea of a fatty degeneration.

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* Virchow, *op. cit.* p. 507. Cf. Waldeyer, *ibid.* p. 322.

† Howse, reported by Hilton Fagge, *Trans. of the Path. Soc. of Lond.* 1873, Vol. xxiv. p. 244.

The greater number of observers, beginning with Dr. Pavy, maintain that there is great over-growth of fibrous tissue in xanthelasma, and on this ground Virchow has proposed to call it *Fibroma lipomatodes* or *molluscum lipomatodes*. In my own case the overgrowth of the connective tissue was not so very apparent: neither does it seem to have greatly struck Waldeyer. A very great development of the fibrous element of the connective tissue would seem incompatible with great cell growth; and xanthelasma, as felt by the finger during life, does not give the impression of hardness. It is probable that one of the distinctions between the flat and tubercular varieties of xanthelasma lies in the amount of connective tissue present.

Another point in which observers differ is the thickening of the cuticle over the patch. Leber* and Dr. Frank Smith† found an increase in thickness of the epidermis; Dr. Murchison found no change in the epidermis,‡ an appearance also met with in a case which I had the opportunity of examining.§ Mr. Howse, indeed, in some specimens of xanthelasma taken from the trachea found no epithelium over the patches, an appearance doubtless due to changes after death, yet some evidence that no increase of epithelium existed during life.‖

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* Leber, *loc. cit.*

† Frank Smith, *Journal of Cutaneous Medicine*, 1869, Vol. iii. p. 244.

‡ Murchison, *Trans. of the Path. Soc. of Lond.* 1869, Vol. xx. p. 191.

§ See p. 333 of this work.

‖ Howse, *loc. cit.*

Within the last twelvemonth Chambard has published a further account of the histology of xanthelasma. His description of the tubercular and plain varieties of xanthelasma differs but little from that given by former histologists; but some details are added as to the state in the tubercular variety of the vessels and nerves, which, he says, have not yet been described. The arteries show an endo-arteriitis, which may block up the bore of the vessel, and the peri-arteriitis, with an active formation of connective tissue, is especially well-marked. The nerve-tubes are soldered together, and the tissue much thickened. Chambard thinks that this implication of the nerves in the xanthelasma tuberosum explains the pain and itching which are felt in this variety, but not in the plane.[*]

It would seem that the diagnosis of xanthelasma ought always to be easy. The only other skin disease with which it may be confounded is milium or comedo, and from this, xanthelasma may be distinguished by the ready enucleation of the contents of the sebaceous cyst when the skin over it is divided, while nothing can be squeezed out of the patch of xanthelasma but blood and a milky fluid. I do not feel at all confident that some of the appearances figured by Mr. Hutchinson as xanthelasma are not milium. One of the patches has a sebaceous plug in its centre.[†] It is plain therefore that the diagnosis is not always one which can readily be made.

As to the possible disappearance of xanthelasma multiplex, I have seen a large crop of xanthelasma tuberosum, planum, and lineare completely disappear in three years, and leave no trace or scar behind, so that it could not be thought that the skin had been the seat of such extensive changes, and this without any change in the jaundice. As the eyelids are the first to suffer, so they appear to be the last to recover, as in this case the man still showed well-marked patches (though much smaller) near the inner angle of the eyelids.[*] In one of Dr. Hilton Fagge's cases the patient told him that some of the patches had disappeared, apparently in a fortnight;[†] but on comparing her state with notes taken before, it rather appeared that the disease was aggravated. In Dr. Frank Smith's case the patches certainly grew less.[‡]

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[*] Chambard, *Bulletin de l'Académie de Médecine*, 1878, 42me année, p. 1173.

[†] Hutchinson, *Med. Chir. Trans.* 1871, Vol. liv. plate iii. fig. 2. Kaposi shares the doubt expressed in the text. (Hebra's *Hautkrankheiten*, 2te Auflage, in Virchow's *Handb. d. spec. Path. u. Ther.* Stuttgart, 1876, p. 252 note.)

As to the treatment of xanthelasma, no drug is at present known to have any influence in removing the spots. Excision by the knife is certainly to be avoided, especially in the neighbourhood of the eye, where the healing of the wound may lead to eversion of the eyelid.

Hydatids of the Liver, Omentum, and Recto-vesical Pouch: Jaundice: Xanthelasma of the Tongue, Eyelids, and Skin.[§]

Charles Kingsley, aged 35, a cattle-dealer, married, came to me in September, 1873, at S. Bartholomew's Hospital, as an out-patient. He was then deeply jaundiced, and had been so for nine months. He said he was not a drunkard, and had not had syphilis. He had never felt any pain in his right side. The urine gave a very marked reaction with Gmelin's test. The left lobe of the liver was much enlarged, even down to the umbilicus. The surface smooth, but the edge sharp. There was well-marked xanthelasma palpebrarum, and there were also two yellow spots the size of pin-heads on the palpebral conjunctiva of right eye, and one like these on caruncle of left. There were spots of xanthelasma on palms of the hands and left elbow, on the right ear and left side of the nose. The tongue was purplish; along its sides were patches, yellowish white, oblong, quite soft, but slightly raised: also a yellow spot on the middle line of the roof of the mouth, and another near the lingual vein. (See No. I. of the chromo-lithographs.)

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[*] See p. 337 of this work for the case at length.

[†] Hilton Fagge, *Trans. of Path. Soc. of Lond.* 1868, Vol. xix. p. 438.

[‡] W. Frank Smith, *ibid.* 1877, Vol. xxviii. p. 236.

[§] This case has been published in the *Trans. of the Path. Society of London*, 1874, Vol. xxv. p. 155, and in *St. Bartholomew's Hospital Reports*, 1874, Vol. x. p. 244.

This patient was admitted into Matthew's Ward on November 18, 1873.

Dr. Herbert Taylor, who was then house-physician, has furnished me with the following clinical notes.

On admission, the patient said he was quite well up to last October twelve months. He was never jaundiced before that time. He then began to feel weak and depressed, and about the same time he was told he was becoming yellow. During these twelve months he had had remissions of the jaundice, remaining clear-coloured for three or four days together. Such remissions have occurred about twice in a month. He has not suffered any pains whatever till the last six weeks; then, about ten minutes after taking any meal, he is seized with pain as though his bowels were being tied in a knot, at the same time his belly swells, and he suffers from wind. The pain lasts from half an hour to three-quarters. For the last six weeks he has had difficulty in passing his stools, and with this, occasionally a little blood with straining. The stools are always clay-coloured and hard, even in the remissions of the jaundice. Micturition during the last week has been very painful; a small stream, occasionally stopping. Before this the urine was abundant, always dark, and staining the linen, even in the remissions of jaundice.

He has lost flesh considerably during the last year; he thinks about two stone. He has not been a spirit-drinker, but has taken much beer.

His legs began to swell about five weeks ago; they are now much less swollen. His skin does not itch much, chiefly the head itches.

Has always been a healthy man, although exposed to all weathers.

He is married, and has six children. He has never had gonorrhœa.

November 19. A thin, care-worn man, blue eyes, sandy-red hair; lying most comfortably on his back. The whole body coloured of an uniform dark yellow tint. Conjunctivæ yellow, pupils contracted. He does not see nor has he ever seen yellow. On certain parts of his body are patches, irregular in shape, assuming more the form of the parallelogram than the circle, of a pale yellow-white colour, paler than the surrounding integument, denser to the touch, but moving freely with the skin over the subjacent textures; smooth surface, not raised; in size from 1 line by 2 lines to half an inch by half an inch. The parts thus affected are: the inner canthus of each eye and adjacent skin, one in palpebral conjunctiva of left lower eyelid, one larger over right temporal region (zygoma), on the helix of the right ear, on the nape of the neck; many small patches on ball of thumbs, one on ball of left little finger, ulnar extremity, around the root of the penis at junction of skin of scrotum with abdomen, and in the perinæum; none below this point; in the flexures of the fingers of both hands, but not in the toes; stains of old purpura on lower arms and the legs. Scattered over the abdomen and back, scantily, are pustules, broken down by scratching. In the mucous membrane of the lower lips are two small patches, similar in appearance to the patches seen on the skin. Along each side of the tongue, reaching from behind forwards to the tip, not appearing on the upper surface, are masses of tissue of similar appearance, somewhat symmetrical.

Pulse 72, regular; radial artery atheromatous; temperature 97·8° F. Chest well formed, movements equal on both sides. Heart's apex beats in the third left intercostal space, half an inch above and to inner side of left nipple. Sounds normal. Resonance good from above downwards to lower border of third rib or third interspace on right side; from that level down to two fingers' breadth below margin of cartilages is dulness. On the left side resonance downwards to level of heart's apex; from thence dulness downwards beyond the cartilages to a level of one and a half inches above umbilicus. Posteriorly the liver dulness encroaches on the chest; good breathing sounds over area of resonance.

Abdomen: distended, resonant below the limits of dulness just described down to the pubes and to each iliac fossa, except in left iliac fossa, where is an area of semi-dulness, oval in outline, corresponding to an area of resistance to the touch, which is not so in right iliac fossa. Splenic dulness nil. The dulness in the epigastrium and hypochondria above described corresponds to a tumour which is felt in that situation, the margin of which reaches from the lower border of the ninth costal cartilage on the right side, passes horizontally inwards to middle line, and then passes vertically downwards to an inch and a half above umbilicus, and again extends horizontally to cartilages on left side, where it is lost. Surface smooth and firm. The edge on the right side is thick, on the left quite sharp and firm. There is also a small umbilical hernia, which he has noticed only for a fortnight.

There is a considerable œdema of the feet and ankles.

November 20. Slept fairly, tongue furred, white, moist; very thirsty, good appetite; no nausea. Pulse 76; temperature 97° F. Urine deeply coloured by bile, sp. gr. 1012, acid, a slight cloud of albumen; griping abdominal pain.

21st. Slept badly; no pain; tongue clean, moist. Bowels open twice. Pulse 76.

22nd. Slept well; bowels acted with pain. Pulse 80; temperature 98°.

24th. Slight pain in belly. Pulse 80; temperature 96·6°.

December 1. He has been sitting up during the week; he feels easier; there was more difficulty yesterday in passing his water. A restless night. Tongue clean, moist, red; œdema of legs and feet has increased. Pulse 80, full and regular.

2nd. Slept well; no pain. Slight tenderness in right hypochondrium; vomited this morning after breakfast; tea makes him sick. Pulse 80.

4th (10·30 A.M.). Slept very badly. This morning there is slight wandering; very severe pain over lower abdomen, right groin, end of penis, and down right thigh. He lies coiled upon his left side. Micturition painful; a small stream, but it does not stop in passing; urine, no albumen, bile-stained. Belly very tender; tongue parched, furred; thirsty, drowsy; bowels open. Pulse 130, respiration 30, temperature 106°. At 2 P.M.—Pulse 135, temperature 105·6°. Lies on his right side; knees drawn up; has passed water since the morning.

10·30 P.M. He is quite unconscious. Temperature 102·4° F.

5th (2·30 P.M.). Quite unconscious. Pulse 144; temperature 105·4°.

He died at six in the evening.

Examination eighteen hours after death. Body of a universal deep yellow, and wasted; shins and feet œdematous. Rigor mortis well marked; the veins in skin covering iliac fossæ, Scarpa's triangle, and front of chest already shown by purple lines. No other signs of decomposition.

Well marked xanthelasmic patches on eyelids, right ear (one of these is covered by a scab of dried blood), scrotum, bend of elbows, flexures of hands, neck, and shoulders. Along the furrows of the hands they are seen as long, narrow lines. Over belly are three or four spots covered with dried blood. No other ecchymoses on skin.

Calvaria is natural; dura mater of a deep yellow; longitudinal sinus empty. Membranes and arteries of brain natural; so also ventricles, central ganglia, and rest of brain.

The inside of body quite warm. A layer of fat under skin. The cartilages are white, the ribs green. No fluid in either pleura. A greenish fluid in pericardium. The heart's apex is on the level of the lower border of third rib, or upper part of third interspace. All the contents of the chest are pushed upwards.

The heart natural; aortic and mitral valves somewhat atheromatous: lungs natural.

Tongue: there is a yellow raised spot, the size of a mustard-seed, on the dorsum. Along each side there are three or four irregular yellowish-white spots. They are sharply defined, varying in size from split peas to a sixpence. Two of those nearest the tip show a loss of substance, and they are also covered with a crust of dried blood. The under surface of the tongue shows two or three yellowish spots the size of mustard-seeds.

The soft palate, pharynx, and lower parts of the œsophagus are free from yellow spots. Just where the œsophagus begins is a cluster of numerous yellow spots for about an inch. There is a yellow spot the size of a mustard-seed at the forepart of the larynx, where the two vocal chords meet. The ridge of the bifurcation of the trachea shows a yellow spot. The rest of the larynx, trachea, and bronchial tubes, which were carefully examined, show no yellow patches which could be confounded with xanthelasma.

The peritonæum, covering the recti on both sides, is speckled yellow with small patches. They are tolerably numerous, and in clusters. Other parts of the peritonæum do not show this appearance.

The great omentum is adherent to the distended bladder. To the left there is a swelling of the size and shape of a grown-up man's kidney. It is within the omentum, but is adherent also to the sigmoid flexure of the colon. Opened it is found to contain an hydatid cyst, which encloses very many small daughter cysts, varying in size from a mustard-seed to a large marble.

The stomach and small intestines are natural. There are no yellow patches either on their mucous or peritonæal surface. The contents of the small intestines quite colourless. The contents of the large intestine are also white and solid; but in many places they have a coating of clotted blood. The mucous membrane of the large intestine from the cæcum to the sigmoid flexure shows innumerable ecchymoses, very fine, and surrounded with fine injection. The rectum natural. Contents colourless, solid, unstained by blood.

The bladder is dilated; it holds about a pint of urine, almost black. This urine gives a decided cloud on applying heat and nitric acid. There is a well-marked green colour with Gmelin's test. It contains urea; something over ·6 *per cent.*

Filling the pelvis between the bladder and the rectum, and making the removal of these organs difficult, is a tumour the size of a child's head. It proves to be another hydatid cyst, but contains no daughter cysts.

On dissecting the porta of the liver, the portal vein is found to contain fluid blood. Swollen lympathic glands surround the bile-ducts. The common bile-duct is quite free from colour; so also the cystic. The gall bladder contains about an ounce of a slightly viscid, colourless fluid. This fluid is rendered cloudy by acetic and nitric acids; it is rendered more viscid by caustic soda. Gmelin's and Pettenkofer's tests repeatedly applied give no trace of colour. Half an inch above the opening of the cystic duct, the canal of the hepatic duct is completely obstructed by a swelling from within the liver. Just before the obstruction becomes complete, the duct contains a semi-solid mass of green pigment. The duct then passes over the wall of the tumour, and cannot be traced for about an inch. Dissecting beyond the tumour, the hepatic duct, dilated to the size of a man's middle finger, and containing a colourless fluid, is open. It receives many large openings of dilated bile-ducts, which also contain a colourless fluid. Following by dissection these ducts, it is found that those in the left lobe are more dilated than in the right. From those ducts in which the surface has been scraped immediately after their being opened, the scrapings under the microcope show abundance of well-formed cylindrical epithelium. No cylindrical epithelium can be seen in the scrapings from those ducts which have been washed with water or touched with a sponge.

Although the large ducts contain a colourless fluid, and are quite white, yet this is not the case with the smaller. They are stained a pale yellow, and on pressing the liver a yellow fluid can be made to come out of them. No yellow spots can be noticed in any of those opened.

Lying in the body, the left lobe of the liver passes for nearly two inches below the level of the right. Taken out, the liver weighs 140 oz. Its colour is a deep olive green, mottled with yellow; surface smooth. On the upper surface of right lobe, near suspensory ligament, are seen two irregular spots, about the size of penny-pieces, of a yellowish colour; they exactly resemble the spots which may be made by pressure on a natural liver after death. A similar spot exists farther back on the upper surface. A cyst projects at the back of the liver, where it is attached to the diaphragm, in the line of the suspensory ligament. The cut surface of the liver is granular; consistence tough.

There are three hydatid cysts in the liver. The largest, about the size of a cocoa-nut, occupies almost the entire thickness of the right lobe of the liver; presses below on the hepatic ducts and on the upper surface of the liver; it is within half an inch of the peritonæum, and causes the yellow anæmic spots before mentioned. Its contents are colourless; no daughter cysts. Another cyst, the size of an orange, lies immediately behind the first, and contains shrivelled-up membranes and a quantity of dark solid pigment. This cyst communicates directly with the hepatic duct by a short canal, about half an inch long and of the diameter of a fourpenny-piece. The third cyst lies at the back of the liver, and projects to the surface where the liver is attached to the diaphragm in the line of the suspensory ligament. Its contents are colourless; no daughter cysts.

Spleen large; very soft. At one end many yellow spots on capsule.

Kidneys large; cortex broad, swollen; white opaque bundles, perpendicular to the medulla, are seen a amidst reddish tissue. The pelvis and ureter of left kidney are much dilated.

Aorta somewhat atheromatous; carotids and iliacs free from any appearance of atheroma or xanthelasma.

The liver-cells were examined with the microscope within an hour of the liver being taken out of the body. Specimens were taken from many parts of the right and left lobes. The cells were all found to present the same characters. Their size and shape were not much altered, but when seen in groups it was difficult to make out their outline. Their contents were chiefly pigment arranged around the nucleus, which was large and contained nucleoli. There were but few fat granules, and no large oil-drops.

Parts of the liver were hardened in spirit and in chromic acid. The increase of the connective tissue in the portal canals was certainly marked, although it was not great. The connective tissue within the lobules was not increased. There were no lymphatic bodies or nuclei present in the connective tissue. It is rare to see so slight an increase in the connective tissue of the liver in cases of long-standing obstruction; the slight increase may be attributed to the nature of the obstruction, the fluid pressure of hydatid cyst.

The patches of xanthelasma were hardened in spirit, embedded, thin sections made with a razor, coloured with carmine or logwood and mounted in glycerine. On examining them with a low power, the cuticle over the patches was seen not to be thickened. In the deeper layers ot the subcutaneous connective tissue were seen lengthened streaks of oil globules. In some specimens there was an accumulation of oil around the air follicles, vessels, and other structures passing through the skin; in others, not. These structures, also, did not seem to share in the disease. The papillæ of the skin seemed affected; that is, the collection of oil drops did not enter the papilla, although it became slightly curved towards it, as it passed underneath.

Examined with a higher power and in preparations teazed out with needles, the collections of fat drops were found to contain cells of various sizes. The smallest were not larger than red blood-corpuscles; round, oval, rhomboidal, and inclined to be spindle-shaped. The smallest were free from granular contents and showed only one or two nuclei. Those larger were slightly granular. The largest of all were four or six times the size of the smallest; round, or oval in shape; showing no nucleus and filled by fat, not in many drops but in one large drop, distending the cells. The cells were separated from one another by fibres of the connective tissue, which seemed to be scarcely much increased. Some of the large fat-containing cells had a sinuous appearance, their shape being apparently determined by the fibres.

The yellow patches under the peritonæum differed much from the patches of xanthelasma. The spots were formed by a spindle-shaped cavity in the connective tissue under the peritonæum, holding large ordinary fat cells, supported by an areolar network. The patches under the peritonæum differed essentially from xanthelasma, and were mere local accumulations of fat in the meshes of the connective tissue under the peritonæum.

Jaundice: Xanthelasma Palpebrarum.

Catherine Lynch, 18 years of age, came to St. Bartholomew's Hospital on Oct. 22, 1873, being kindly transferred to my care by my friend and colleague Dr. Lauder Brunton.

She came to the Hospital on account of her jaundice which has lasted over 12 months. She came again on Oct. 30, when she was questioned more at leisure. She then said that she had been ill for 2½ years with feelings of heaviness, sleepiness, and sickliness. She had noticed a swelling in the belly for 2 years and a month. She had menstruated but once; that about fourteen months ago, and the discharge was then very little; she had enjoyed tolerably good health up to the time of falling ill. She had been jaundiced more than fourteen months, but the yellowness had been growing less for the last six months. The urine brought was not highly jaundiced but gave a distinct green ring with Gmelin's test. Before last week, she said, the motions were yellow; this week they have been very dark.

Examining her more narrowly, she was found to be only slightly jaundiced. There were two symmetrical lines of xanthelasma along the inner half of both lower eyelids; the patches were oval in shape, and their long axis vertical, smooth and soft. She had noticed them for six months. No other patches of xanthelasma were noticed over body or hands. There was a large phlyctenula and much injection of right eye. Also a swelling about the size of a pigeon's egg, elastic, almost fluctuating, in the left parotid region had been noticed for two years. The lymphatic glands below were enlarged. The left tonsil was enlarged; not so the right. The glands in the axilla enlarged; not in the groin. Blood examined with microscope showed no increase of the white corpuscles.

There were many sonorous and sibilant rhonchi all over chest; cough very troublesome; phlegm abundant and yellow. Heart-sounds natural.

The liver was enormously enlarged. Its edge was very hard and could be plainly felt in the right iliac fossa; then the edge began to ascend to the right of umbilicus; about an inch above which is the notch, and the left lobe then passes away along the epigastrium till it be lost under the ribs. Surface of liver generally smooth; but midway between lower border of liver and lower border of ribs is a rounded swelling on surface of liver, smooth and highly elastic. Spleen large and moveable. Belly tender when handled.

Father is a porter at Covent Garden. When a child used to eat abundantly of raw vegetables; but not lately.

She was told to take a draught containing fifteen minims of tincture of squills, and the same of paregoric in an ounce of infusion of cascarilla every four hours, and to stay altogether indoors in a warm room.

She came again on Nov. 3. The cough was much less although she still felt sick after a paroxysm. The jaundice also less and motions reported to be a bright yellow.

On Nov. 6, the elastic tumour in parotid region seemed smaller. It was found to be placed a little behind the ear, more over insertion of sterno-mastoid. There was a swelling also not distinctly circumscribed of whole parotid region, even over the masseter. She had never noticed any change in power of discerning colours: white things, for example, always looked white. Liver unaltered.

On Nov. 10, the cough was altogether gone; but the jaundice was somewhat deeper: the urine also gave a more decided reaction with nitric acid. She was ordered to take a draught containing dilute aqua regia before meals.

On Nov. 17, the jaundice was less marked, and there was less intense reaction with nitric acid on the urine. Still the jaundice was marked although slight.

It was noted on Nov. 27, that the elastic tumour on the liver seemed larger; it was about the size of half a good-sized orange; it was now only a finger's breadth from the lower margin of ribs, and stretched nearer the left edge of right lobe. Pulse 96, standing. The phlyctenula now began to be more troublesome, and in consultation with Mr. Howard Marsh, it was determined to blister her behind the ear. Several spots of erythema nodosum were noticed on arms and one spot on shin; but no more xanthelasma. To take two teaspoonfuls of cod-liver oil three times a day.

On Dec. 4, the eye was better: the liver as before.

On Dec. 11, the eye was again not so well. She was therefore sent to see Mr. Power, the Ophthalmic Surgeon. Since that time, I have not seen her nor have I been able to gather any information about her.

Jaundice: Xanthelasma Multiplex.[*]

Mrs. C. aged 36, was an out-patient at S. Bartholomew's Hospital under Dr. Andrew in the spring of 1868.

The patient has been married 17 years. She has had 9 children, the youngest 14 months old, one is dead. She has had 3 miscarriages. Two years ago last December she had a quarrel with her husband and a very great fright; and about a week after, she began to turn yellow. They were then living near Aberdeen, and it would seem that she had had much anxiety and annoyance for some time before. For the last three years she had been subject to flooding. The spots began to appear about six months ago, and were first noticed on the elbows as little spots the colour of the skin. She has had much itching and irritability of the skin, which came on about two months after the jaundice but is not nearly so bad now. At one time she used to be obliged frequently to sponge in cold water, and could not sleep at night. The spots are most abundant on the elbows, palms, and soles; but on the palms, (soles not seen) they are very slightly, if at all elevated, resembling rather opaque spots in the skin, which presents a marbled appearance from the very great number. She does not sleep well, but does not know why. The tongue is clean: the appetite uncertain; she used to be fond of fat, but cannot take it now. The bowels are regular, slightly costive. Motions during illness have been light coloured, but for the last three weeks, they have been almost natural. The urine is said to be high coloured. The pulse is 60. She has lost nearly four stone in weight, she used to weigh fourteen stone.

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[*] This case has been published before in *Trans. of Path. Soc. of London*, 1874, Vol. xxv. p. 259.

Two or three weeks ago she passed something hard at stool, (? gallstone), and her present improvement seems to date from that. Her complexion is now lighter and the spots are less than they were a few weeks ago.

Jaundice: Xanthelasma Multiplex.

James Piggott, aged 32, came to Saint Bartholomew's Hospital Sept 24, 1873.

He says he is unmarried, but that he has never had syphilis or gonorrhœa. He has been a teetotaler since 1863. He has always enjoyed good health; in 18 years he has only been away from business 2 hours owing to ill-health.

He has been jaundiced now for three months. He has been over anxious of late about business.

Present state. The colour of the skin is a deep sallow unlike ordinary jaundice: the conjunctivæ are blood-shot, and do not at first sight strike observer as being icteric. On close examination they are plainly so. The urine high coloured, but contains no albumen, and on being tested with nitric acid in Gmelin's way, there is no trace of a green colour, nothing but a red ring above the nitric acid is found. The stools are said to be now of a fawn colour; under the club doctor they were dark. Liver dulness (absolute) begins two fingers' breadth below nipple and reaches down to the level of the umbilicus. The liver can be felt below this: it does not cross middle line. It is slightly tender to feel: its surface smooth, save just below the junction of the ribs and cartilages, where a rounded smooth swelling size of a small apple may be felt. The belly somewhat retracted: not tender generally. The pulse is 18 in 15", intermittent about 1 in 18.

There is much itching especially about the thighs at night. He does not complain of any pain. His chief trouble is his weakness and loss of flesh.

To take the nitro-muriatic acid draught.

Oct. 8. Liver dulness as before. Epigastrium slightly tender. The splenic dulness is enlarged and the tip can be distinctly felt under ribs. Pulse 22 in 15", not intermittent but very small. There is no murmur at heart; second sound at base reduplicated. Weight remains about the same.

Oct. 11. The edge of the liver is rounded to feel; motions of a light yellow colour. The conjunctivæ are now markedly jaundiced; the urine bilious, but contains no albumen. A beautiful green reaction is given with Gmelin's test.

Oct. 15. He ate two pears yesterday and has been much purged; does not feel so well in consequence. Jaundice the same. There is no xanthelasma palpebrarum.

Oct. 29. Epigastrium still tender. Liver dulness as before; edge as before; the rounded swelling as before. Jaundice somewhat less. Pulse 18 or 19 in 15". The urine shows no albumen, but a slight green reaction with nitric acid. There is no xanthelasma to be seen anywhere. The man says he feels stronger; tongue very red, cracked across. He goes to-morrow to St. Ives to live.

Dec. 3. He came up to-day from St. Ives, where he has been for the last six weeks. He says he has gained 2 or 3 lb. in weight, but he still complains of itching; the jaundice is now only slightly marked; the urine on the other hand very highly coloured; on boiling and adding nitric acid a faint cloud appears; there is deep green reaction with nitric acid. There is a general bulging of the lower ribs on the right side. The deep liver dulness begins at nipple, but is not absolute for two fingers' breadth below. The dulness now extends below ribs for three fingers' breadth. Tympanitic sound to the left of the middle line. The liver can be felt almost to level of umbilicus. Tip of spleen also distinctly felt. Pulse 20 in 15", not intermittent. Stools now light drab.

Has noticed no changes in perception of colours since illness. The conjunctivæ are much injected. A few yellow spots size of pin's point around inner canthus of eyes.

To continue the draught of nitro-muriatic acid.

Aug. 12, 1876. He came to see me again. For several months past he has been living in North Staffordshire, working at the pottery business. He is in London for the day.

He has now well marked xanthelasma multiplex. There are large symmetrical patches on the inner aspect of both eyelids of the plane variety. On the upper right eyelid is a tuberose patch size of a pea. There is none on the face or head, if a doubtful spot on the lower lip be excepted. None on front or back of trunk, until the cleft of the nates be reached; on each side of the upper part of this cleft is an abundant crop of prominent tuberose xanthelasma. In the middle line of the sacrum there is an oblong patch of xanthelasma planum. On the arms there is none, save about both elbows; the olecranal surface is studded with the tuberose form; the flexure with the plane. There is one small tuberosity on back of right hand; the flexures of both palms and of the fingers are marked by broadish lines of linear xanthelasma.

There is a patch of plane xanthelasma at base of penis and another in middle line of perinæum. There is none on the thighs and legs. But on the left sole, just where the great toe joins the foot, is a streak of linear xanthelasma.

There is no xanthelasma on tongue; nor as far as can be judged on gums. He wears false teeth.

He has been slightly jaundiced since his last visit. He scratches his thighs much, but says this is due more to habit than real sense of itching. Conjunctivæ still coloured yellow; but the complexion is very peculiar, not jaundiced, but very dark; in a healthy person it would suggest an infusion of black blood. He has black hair. The urine is high coloured and looks bilious. It does not stain white paper yellow, nor does it give a green colour with nitric acid. After being boiled, nitric acid causes an opalescence.

He says he first began to notice the xanthelasma in his hands, the spring of this year; he does not remember in what month. He thought they were due to the cold weather. He has been jaundiced continuously for three years.

The liver dulness now begins two fingers' breadth below nipple and reaches to a finger's breadth above border of chest. In axillary line it reaches to border of chest. It cannot be felt, neither can spleen. The tongue is red and fissured. The appetite is bad. He, however, considers himself stronger and better than he was three years ago.

He was heard from on Jan. 4, 1877: he said: "The white marks upon my hands are less plain, but I have such a habit of rubbing myself and rubbing off any little scar or head which are (*sic*) felt moist when warm."

Oct. 18, 1879. He again reported himself to day. He is still slightly jaundiced and looks thin. He is able to do some light work, such as that of a clerk or book-keeper.

The patches of xanthelasma have everywhere, save on the eyelids, disappeared. The palms of the hands, the elbows, the nates and sacrum, penis and perinæum, and the left toe, are free from all traces of the disease. The skin is quite smooth and supple, and it is hard to believe that it has been the seat of so extensive a pathological change. Over the elbow there is some roughness, but it is doubtful whether it be more than is common; and there are one or two scars, caused, he says, by his tearing the tubercles out with his nails, which then bled plentifully.

He cannot remember the exact time at which the patches began to go away, but thinks it was about the beginning of 1877. No treatment was adopted with a view to their removal.

There is still the same marked bulging of the lower right ribs, and the liver's thin edge can be felt just under the margin of the ribs; the spleen can also be distinctly felt. The liver dulness begins three fingers' breadth below nipple line, and at the same distance in parasternal line, but very quickly is succeeded by a tympanitic sound.

The urine is still bilious to the eye, but gives no distinct Gmelin's reaction.

CHAPTER XIII.

THE MORBID ANATOMY OF JAUNDICE.

THE body of a person who has died of jaundice very readily decomposes. Even in cold weather, the veins over the belly and thighs may be seen as purple streaks within 24 hours of death. The *rigor mortis* rapidly disappears.

The jaundice of the tissues noticed during life persists after death. Gubler thinks that it is the fibrous tissues only which become stained in jaundice by a sort of elective affinity, like that of madder for young bones.*

Certain tissues remain free from colour even in the most intense jaundice. Such are: the teeth, the hair, the brain, the humours of the eye, the cartilages, an appearance which may specially be noticed in the costal cartilages; not so well marked when the body is first opened, but it may well be seen when the bile pigment in the ribs has been oxydised by the action of the air into biliverdin; the cartilages remaining whitish, while the ribs are deep green. The absence of colour in the teeth and cartilages may be readily explained by the absence of large blood-vessels in their structure. It is not so easy to explain the absence of colour from the nerve-centres and nerves themselves, which are always white.† The fluid in the meninges and in the ventricles of the brain may be deeply yellow, while the substance of the brain itself is free from colour.

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* Gubler, in Michel, *De l'ictère hémaphéique*, Thèse de Paris, 1868. p. 8.

† Dr. Murchison (*Lectures on Dis. of the Liver*, London, 1868. p. 285) says that the jaundiced tint penetrates the brain. This is quite contrary to my own experience and to the statements of nearly every other writer that I have consulted. Frerichs indeed says that the brain, when œdematous, may have a yellowish appearance, but this is clearly due to the unnatural presence of serum in the brain, not to the colour of the brain itself.

It is worthy of note that in some cases of secondary malignant tumours in the liver, where the primary tumour, such as cancer of the head of the pancreas, has caused a jaundice, the secondary tumours in the liver are not stained, though in the midst of a highly jaundiced organ. This fact may be compared with the same absence of colour in the fluid of the gall bladder and gall ducts after long-standing obstruction.

In jaundice the first organ to suffer is the liver and its ducts, and to this part of the body the attention of the morbid anatomist must be at first directed. It is of the utmost importance, as Virchow has pointed out,[*] that the examination of the ducts leading from the liver, the hepatic and common duct, should be made in a particular fashion, otherwise the results gained are of little or no value. The object of the examination is to test the patency of the common duct. This used formerly to be done by opening the duodenum near the orifice of the common duct, and then pressing upon the gall bladder. If the contents of the gall bladder passed into the duodenum, the ducts were judged to be patent during life. This test is exceedingly rough, and cannot be trusted either for negative or positive results. In the first place, if no bile flow out, it does not show that the common duct is obstructed, as the cystic duct may be plugged, and thus no bile from the bladder may pass into the gut; in the second place, if bile flow out, it does not show that there was no obstruction during life, as catarrh, hyperæmia, and œdema, of the mucous membrane of the common duct readily enough disappear after death, while during life a serious obstruction may have existed. Lastly, it does not exclude obstruction of the hepatic duct.

The same objections may be made to the passing of a probe up the duct from the papilla, and seeing if there be any obstruction which cannot be overcome. An improvement on both the foregoing methods is the plan of laying the duct open, and seeing if any gross obstruction, such as a plug of mucus, or tumour pressing on the duct, exist. But in all cases, however, the following will be found a better way: in opening the belly great care must be taken not to disturb or press on the gall bladder or ducts. The large intestine and omentum may be carefully removed, and raising the liver without pressing on the gall bladder, the common and hepatic ducts may now be dissected out. It is most convenient to open the common duct a little above its passage into the duodenum, and with a probe-pointed pair of scissors to follow it first downward into the gut, and then upwards towards the liver. Great attention must be paid to three points in the state of the duct: i. a swollen state of the mucous membrane; it is well known that hyperæmia of mucous membranes readily disappears after death, just as the redness of erysipelas of the skin is lost, and the only *post mortem* signs are the swelling and œdema: ii. a plug of mucus and epithelium at the opening of the duct into the intestine; if this be white and not stained by bile, it is proof that no bile has passed along the duct since the plug was formed: iii. a colourless state of the lower part of the duct near the intestine, while the upper part is stained yellow by bile. This is most important evidence, as it shows that no bile has passed down that part of the duct which is unstained by bile, at all events for several days before.

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[*] Virchow, *Arch. f. path. Anat.* 1865. Bd. xxxii. p. 117. Cf. *Wien. med. Wochenschrift*, 1858 No. 24.

I have sometimes found that the mere movement of the body after death, such as is necessary in carrying it from one room to another, is enough in some cases of jaundice to send the bile from the gall-bladder down the ducts. Some time ago I was examining a case of pneumonia complicated by jaundice, and used great care that no pressure should be made on the gall-bladder. Yet on opening the ducts, common and hepatic, they were found deeply stained with a fluid of the same colour and appearance as that in the gall-bladder; no obstruction was found in the ducts or at the papilla. The contents and mucous membrane of the duodenum were stained yellow for about three inches above and below the papilla; but beyond this narrow strip, the contents and wall of the intestine, above and below, were perfectly free from all bile staining. The contents of the small intestine were markedly colourless.

The obstruction to the ducts may also be high up in the liver in the finer ducts, so that they should be carefully dissected, and an obstruction within them may be discovered. Oskar Wyss[*] and Ebstein[†] have shown the existence of plugs of mucus in the fine ducts of the liver in cases of poisoning by phosphorus, in which disease the large ducts of the liver are commonly free and coloured. Cornil has shown that even the finest ducts, those just outside the lobules, may be filled by masses of epithelium, and obstruction to the flow of bile caused in this manner.[‡]

If the obstruction to the bile ducts be permanent and near the duodenum, as, for example, a tumour growing from the head of the pancreas, the ducts outside the liver are commonly found much dilated. The gall-bladder suffers very early and becomes much distended. The ducts themselves may often be seen as large as, or even larger than, the middle finger. In man they do not seem to become tortuous; but it is not uncommon to see this appearance in animals when the ducts have been tied near the duodenum. They may attain an enormous size. As an instance of this, there is a case which has become quite classical, because quoted by Morgagni. It is a case by Traffelmann, who found in the body of Daniel, Archbishop of Mainz, that the bile ducts were filled with gall-stones and dilated *instar utriculi.*[*] Morgagni, in quoting this, has changed the *utriculi* into *ventriculi*,[†] and every writer up to the present day has quoted this case as one of dilatation of the bile ducts to the size of a stomach. There are, however, well authenticated cases in which the dilatation of the ducts has been quite as great, if not greater, than that imagined by Morgagni. The most extreme case with which I am acquainted is recorded by Dr. Halliday Douglas. In a jaundiced girl, seventeen years of age, a fluctuating tumour could be felt on the right side nearly as low as the ilium. Thirty ounces of fluid were withdrawn by tapping. On examination after death, a sac was found on the right side of the belly, over the front wall of which the duodenum passed as a flat band. The walls of the sac were dense and fibrous, one twelfth to one eighth of an inch in thickness. At the upper part of the sac, the dilated openings of the hepatic and cystic ducts were seen. The hepatic duct within the liver was much dilated.[‡]

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[*] Oskar Wyss, *Arch. d. Heilkunde*, 1867, p. 469.

[†] Ebstein, *ibid.* 1867, p. 506, and 1869, p. 379.

[‡] Cornil, *Comptes rendus des séances de la Société de Biologie*, 1875, juillet, p. 306.

Todd, of Dublin, found in a girl of 14, the hepatic and common ducts so enormously dilated that they contained more than a quart of bile, and formed a sac which reached from the porta of the liver to the os sacrum. The ducts lay behind the duodenum, pancreas, and the root of the mesentery, and covered the anterior surface of the right kidney and the greater part of the left. The cause of the dilatation was a scirrhous state of the pancreas.[*]

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[*] Traffelmann, quoted by Schenk, *Obs. med.* lib. iii. sect. ii. Lugd. 1644, p. 405. To increase the confusion, the Archbishop is often spoken of as a Prince: it must be remembered that the Archbishops of Mainz were temporal as well as spiritual princes. He was the first of the electoral college of the Roman Empire, and Arch-chancellor of Germany.

[†] Morgagni, *De sedibus, etc.* Epist. xxxvii. Sect. xlvii.

[‡] Halliday Douglas, *Monthly Journal of Medical Science*, Edinburgh, 1852, Vol. xiv. p. 97.

Frerichs gives a drawing of an immensely dilated common duct, which is in the Museum at Breslau.[†]

The ducts within the liver suffer latest. They do not dilate to anything like the size of those outside. This is doubtless due to the liver-tissue preventing any very great dilatation.

The ducts may show uniform or saccular dilatations. The former is no doubt the most common. The left hepatic duct has always appeared to me more dilated in proportion to its size than the right. This is probably due to the bulk of the left lobe being less than the right; thus less resistance to the dilating force is offered.

The walls of the ducts themselves are thickened, even to the naked eye. Under the microscope this thickening is seen to be due to a great overgrowth of the fibrous coat. In this, great abundance of lymphatic elements may be found, just as in cirrhosis. Raynaud and Sabourin have lately described as well distinct layers of muscular tissue in the walls of the dilated ducts outside the liver; but the muscular tissue disappeared as soon as the ducts passed into the liver itself.[‡] Frerichs[§] and Schäfer[||] have been unable to recognise any epithelium on these dilated ducts. Heinrich Mayer,[¶] however, speaks of them; and I myself have seen abundance of cylindrical epithelium in cases which I have examined carefully. Charcot and Gombault seem to consider the retention of the epithelium almost a necessary feature in the anatomy of the dilated ducts; the epithelial proliferation, say they, must be very active, and is a sign of the irritated state of the wall of the duct.* I have little doubt that the absence of the epithelium is a *post-mortem* change; the ducts must not be meddled with before the examination; they must not be washed or wiped, or no epithelium will be found.

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[*] Todd, *Dublin Hospital Reports*, 1817, Vol. i. p. 325. It is worthy of note, as some explanation of the enormous dilatation of the common and hepatic ducts, that in both these cases of Halliday Douglas and of Todd, the cystic duct was obstructed. In Frerichs' case, the gall-bladder was of the usual size.

[†] Frerichs, *Klinik der Leberkrankheiten*, Braunschweig, 1861, Bd. ii. p. 444. He has used symbols, so it is almost impossible for an Englishman to tell what he means by his measurements.

[‡] Maurice Raynaud and Charles Sabourin, *Archives de Physiologie*, 1879, p. 46.

[§] Frerichs, *op. cit.* Bd. i. p. 148.

[||] Schäfer, *De hydrope ductuum biliarium*, Diss. Inaug. Turic. 1842, p. 9.

[¶] Heinrich Mayer, *Mediz. Jahrbb. hrsgeg. von d. k.k. Gesellschaft der Aerzte*, Wien, 1872, p. 139.

The follicles which open upon the mucous surface of the gall ducts are usually found dilated and filled with pigment. Raynaud and Sabourin have paid especial attention to the appearance of these follicles in obstruction to the ducts. They find in the connective tissue of the portal canals numerous little bodies, which resemble the section of small racemose glands, and are scattered without order around the bile ducts. They are made up of tortuous tubules lined with a single layer of cubical epithelium, and opening into the larger bile ducts. Raynaud and Sabourin look upon these bodies as either the normal glands of the ducts much hypertrophied, a view which seems to me the more probable; or else that the very small ducts seen naturally in the portal spaces, are prolonged and rolled up into a ball.† They appear to be quite distinct from the developments of the ducts described by Charcot and Gombault, Hanot and others.

The contents of the widened ducts vary much. If the examination be made soon after the obstruction have been set up, the contents will be found to be bile little altered. Later on, the bile becomes thickened and tenacious, and a kind of biliary gravel is thrown down. Should the obstruction continue long, the colouring matters of the bile are absorbed and leave only a colourless fluid,[*] at first viscid from the presence of mucus, but afterwards limpid. This colourless fluid has been very little examined. There are but few records of the analysis of the colourless fluid found in the gall-bladder, but there seems to be only one case recorded of any chemical analysis of the fluid from the ducts. In this case Schäfer says it possessed all the physical and chemical properties of the plasma of the blood.[†] In two cases which I have examined I found no bile acids or bile pigment in the fluid.

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* Charcot and Gombault, *Archives de Physiologie*, 1876, pp. 275 and 289.

† Raynaud and Sabourin, *op. cit.* pp. 43 and 48.

The presence of this colourless fluid was formerly looked upon as evidence of the cessation of the secretion of bile, of an acholia, an opinion which even a recent writer has supported.[‡] The phænomena are, however, better explained by believing that the fine ducts of the liver have been blocked up by mucus, and thus the bile hindered descending into the larger tubes.

The saccular dilatations of the ducts, and the multiple abscesses of the liver, sometimes caused by obstruction to the ducts, would best be considered under the head of diseases of the ducts themselves.

The state of the texture of the liver itself will next be considered. Soon after the obstruction to the ducts is set up, the liver changes in colour. In some cases of short duration, however, no change in colour is seen. The liver becomes mottled in two shades of yellow, of which the deeper colour is seen in the centre of the lobules, the lighter in the circumference. Under the microscope the mottling is seen to be due to an infiltration of the cells of the liver with granules of pigment, the pigment being most abundant in the centre of the acinus around the hepatic vein. I am not acquainted with any explanation of the appearance of bile pigment in the cells of the centre rather than of the circumference. It has seemed to me possible that as the gall-ducts take their rise from the circumference of the lobule, the cells lying nearest to them may be able to discharge their contents more readily than the cells lying in the deeper parts.

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[*] I fear that I am unable to agree with Dr. Hilton Fagge in his statement that 'in jaundice the biliary passages are almost always found to contain, not bile, but, an almost colourless mucus." (*Guy's Hosp. Reports*, 1875, Vol. xx. Third Series, p. 172). In my own experience the reverse has been the case.

[†] Schäfer, *loc. cit.* The absence of bile acids from the bile found after death in the gall-bladder would seem to be more common than is generally supposed. Golowin (*Arch. f. path. Anat.* 1871, Bd. liii. p. 420.) says that in two out of 36 cases, no bile acids could be found: both were cases of parenchymatous degeneration of the liver and one was jaundiced.

[‡] Moxon, *Trans. of the Pathological Society of London*, 1873, Vol. xxiv. p. 129.

In one of his experiments on the bile, Heidenhain allowed a solution of indigo-sulphate of soda to flow under moderate pressure into the bile duct of a living animal. He found the mucous membranes, the conjunctiva, the serous membranes, and the fasciæ to become blue; and even blue urine was passed. But the liver itself was the organ least coloured. By careful observation it could be seen that here and there between the lobules there was a tinge of colour; the lobules themselves being natural. If, at the end of the experiment, the liver were hardened and examined, only the intra-lobular bile ducts and their neighbourhood were found coloured. And if the experiment were broken off, even where the conjunctivæ and urine had become blue, the liver recovered itself and clear bile was secreted. These circumstances make it evident, says Heidenhain, that absorption does not take place within the canals of the lobule in which the bile is secreted, or otherwise the liver would be quite blue; the intra-lobular ducts of Chrzonszczewsky* would be then coloured; but the absorption must take place in the inter-lobular ducts. The place of absorption is therefore different to the place of secretion. The first takes place between the lobules, the second within them. When in jaundice the liver cells become coloured, it is a secondary not a primary phænomenon, the bile is secreted by the lobules, passed into the intra-lobular ducts and thence into the inter-lobular ducts, through the walls of which it is absorbed, and passes by way of the lymphatics again into the lobules.*

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* Chrzonszczewsky, *Arch. f. path. Anat.* 1866. Bd. xxxv. p. 153.

The readiness with which bodies are absorbed from the bile ducts is shown by the following experiment by Picard. He injected a solution of "prussiate of potash" into the stomach of two dogs in full digestion, but the injection was followed by no symptoms of poisoning. The same drug, injected into the bile duct, caused the death of the animal instantly. It is perhaps worthy of note, that no resistance was felt to this injection, but that it passed as readily as into an empty cavity.†

It was noted by Saunders that after ligature of the bile duct the lymphatics coming from the liver were filled with a bilious fluid;‡ and Richard Powell says that in one case of jaundice he saw evident and satisfactory marks of the presence of bile in the thoracic duct.§ More lately an important contribution to the investigation of the manner in which the bile leaves the liver in jaundice has been made by Fleischl. Working in the Laboratory at Leipzig, Ludwig asked him to notice that, in a dog whose bile duct had been tied, the lymphatics from the porta to the *receptaculum chyli* were distended with a yellow lymph which gave Gmelin's reaction. Taking up the matter as a definite research, he found that if the bile duct were tied, and a cannula inserted into the thoracic duct in the neck of a large dog; that the lymph contained abundance of bile acids, but the blood not a trace. Hence it is concluded that the bile, in cases of obstruction of the gall-ducts, passes out of the liver by the lymphatics into the thoracic duct, and thence into the blood. If both the common bile duct and the thoracic duct be tied together, no bile passes into the blood.*

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* Heidenhain, *Studien. d. phys. Inst. zu Breslau*, Leipzig, 1868, Heft. iv. p. 233.

† P. Picard, *Lyon médical*, 1879, t. xxxi. p. 296.

‡ Saunders, *A Treatise on the Structure, Economy, and Diseases of the Liver*, Lond. 1803, Third ed. p. 112.

§ Powell, *Observations on the Bile and its Diseases*, London, 1800, p. 55.

As the obstruction lasts, so the colour of the liver becomes deeper, and finally of a dark green, the central parts of the acinus retaining the deeper tint, even to the end of the disease. With the increased depth in colour, the liver becomes firmer and tougher, and in the last stages of all shows a distinct granular appearance both on section and surface. The liver, which in the early stage of jaundice showed a distinct enlargement, now begins to shrink; and this shrinking, toughness, and granular look, may be due to one and the same cause, an increase in the connective tissue.

The histological changes of the liver in obstruction to the duct had been until lately but little studied,* though at Paris we are told that within the last three years the subject has become the order of the day. This is no doubt owing to the experiments of Charcot on this point, which have everywhere drawn much attention.

Oskar Wyss was the first to pay much attention to this state, and the greater part of his research was devoted to describing the casts of the inter-cellular bile ducts, which may be seen in some cases of jaundice, but are not very common. He describes numerous green or greenish-brown bodies, of a rounded or lengthened shape, sometimes branched, from 2 to 5 micro-millimeters ($\frac{1}{1000}$ of a millimeter) in diameter, and sometimes reaching 13 micro-millimeters. The bodies are only found between the liver cells, never within them, and sometimes form a complete network between and about the cells.[*] Oskar Wyss looks upon these bodies as casts of the capillary ducts, varicose from distension with bile, an opinion in which most will be inclined to agree with him. I have myself verified his account of these bodies on several occasions, notably in a case of congenital deficiency of the ducts.[†]

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* Fleischl, *Arbeiten aus d. phys. Anstalt zu Leipzig*, 1874. Jahrg. ix. p. 24. He has noticed that many lymphatics leave the liver with the connective tissue of the hepatic vein as well as by the porta.

† The chief writers who have dealt with this point are: Handfield Jones, *Trans. of the Pathological Society of London*, 1854. Vol. v. p. 146. Frerichs, *op. cit.* Bd. i. pp. 122. 139. and 248. Bd. ii. p. 501. Beale, *Archives of Medicine*, 1859. Vol. i. p. 125. Foerster, *Würzb. med. Zeitschrift*, 1861. Bd. ii. p. 161. Klebs, *Handb. d. path. Anat.* Berlin, 1869. Bd. i. p. 425.

There are changes, however, which the cells and the capsule of Glisson undergo, and which it will be convenient to describe separately from one another, and also to consider the changes in the capsule of Glisson before the changes in the cells.

There may be found some signs that the older writers suspected changes in the connective tissue of the liver in cases of obstruction to the ducts. Albers, speaking of these cases, describes the parenchyma of the liver as granular, rough, and coloured yellowish-brown; while in one case, he says, the liver was really cirrhotic: it appears that the cellular tissue of the liver is partly atrophied, partly indurated.[‡] Andral has recorded a case which, although rendered less valuable by the fact that the patient was a drunkard, yet deserves some attention. The bile ducts were much dilated, and the liver was small, deep green, very dense and granular on the surface and section.[§] Yet notwithstanding these hints as to the granular state of the liver, Oskar Wyss was really the first to assert an over-growth of the connective tissue, and yet he passes it by in a few lines, and says that the increase is never very great, and that no increase of the connective tissue within the lobule has yet been seen.[*] I agree, notwithstanding, with Oskar Wyss, that in cases of slight and transient jaundice, the connective tissue of the liver in man is not increased. It is, however, far otherwise when the jaundice lasts long and is severe, or if the cause of the jaundice be one which would beget great changes in the portal canals. Thus, the over-growth of the connective tissue is very great in animals whose bile ducts have been tied. The increase is here so great that the liver closely resembles that of a drunkard; the connective tissue is studded with lymphatic corpuscles just as in cirrhosis, and the new connective tissue enters deeply into the lobules.[†] The same appearances may be met with in man when the obstruction is due to the presence of rough angular gall-stones in the common duct, but especially in those rare cases of congenital deficiency of the ducts. A less overgrowth of the connective tissue may be met with in cases of jaundice from cancer of the head of the pancreas, or tumour pressing upon the liver from the outside. The very least increase of the connective tissue that I have ever met with was in a case of complete obstruction to the hepatic duct by a hydatid tumour. In this case the increase of the capsule of Glisson was so slight that there was a complete absence of the lymphatic corpuscles which are nearly always seen in cases of overgrowth of the connective tissue in the liver. This case seems to me to disprove Charcot and Gombault's theory, that the overgrowth is due to the distension of the ducts,* and an early putrefaction of the bile; for here the distension was carried to the utmost, and yet no cirrhosis arose.

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[*] Oskar Wyss, *Arch. f. path. Anat.* 1866. Bd. xxxv. p. 553.

[†] Wickham Legg, *Trans. of the Pathological Society of London*, 1876. Vol. xxvii. p. 181.

[‡] Albers, *Beobachtungen auf dem Gebiete der Pathologie*, Bonn, 1836. p. 19.

[§] Andral, *Clinique méd.* Paris, 1839. 4e éd. t. ii. p. 534. Virchow (*Würzb. Verhandl.* 1857. Bd. vii. p. 27.) and Liebermeister (*Beiträge zur path. Anat. u. Klinik d. Leberkrankheiten*, Tübingen, 1864. p. 135.) both seem to have looked upon the irritation caused by gall stones as the cause of the increased connective tissue in the liver. Cf. a case by Dr. Henry Green. (*Trans. of the Path. Soc. of London*, 1872. Vol. xxiii. p. 133.)

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[*] Oskar Wyss, *op. cit.* p. 559.

[†] Heinrich Mayer, Stricker's *Mediz. Jahrbb. hrsgeg. von d. k.k. Gesellschaft d. Aerzte*, Wien, 1872. p. 133. Wickham Legg, *St. Bartholomew's Hospital Reports*, 1873. Vol. ix. p. 161. Charcot and Gombault, *Archives de Physiologie*, 1876. p. 272. Foà and Salvioli (*Archivi per le Scienze med.* 1877. quoted in *Centralblatt f. d. med. Wiss.* 1878. p. 600.) have repeated this experiment on many animals of different tribes, mammals and birds, but they have not found any noteworthy changes different from those already described.

It is clear that it is only by means of animals that this overgrowth of the connective tissue in jaundice could be demonstrated. Any similar attempt from the liver of man would always be met by the insinuation that the patient was a drunkard.

The cause of this overgrowth of the capsule of Glisson is obscure. It has been suggested to me that it may be due to the ducts feeling (if such an expression be allowed) the necessity for increased resistance, and thus strengthening themselves by adding fibrous tissue to their walls. This cannot be, however, as in the case just mentioned of hydatid tumour completely obstructing the hepatic duct, there was abundance of dilating force within the ducts, and yet the connective tissue was but little increased in comparison with other cases. I thought at one time† that it was the presence of the ligature in the portal fissure which, in the case of animals, set up a great overgrowth of the connective tissue around the vessels, which extended at last to the liver. In connexion with this view it is interesting to observe that a like overgrowth of the connective tissue is seen when the portal vein has been tied after Oré's method.‡ In fact, an overgrowth of the connective tissue follows many other disturbances of the circulation in the liver, as in nutmeg liver.§ And in the kidney, the same interstitial process is set up where any impediment exists to the flow of urine out of the pelvis. But I have lately met with a case which destroys this theory. In a patient, deeply jaundiced, I found a small cancer, not larger than a hazel nut, placed on the mucous membrane of the duodenum and completely obstructing the flow of bile into the duodenum. Here there was no interference with the connective tissue of the porta; yet the liver was as markedly cirrhotic as I have ever seen it in the cirrhosis from obstruction to the bile.

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* Charcot and Gombault, *op. cit.* p. 289. Dr. Lionel Beale seems in some degree to favour, by anticipation, Charcot's theory in his case of cirrhosis from obstruction. (*Archives of Medicine*, 1859. Vol. i. p. 127.)

† Wickham Legg, *op. cit.* p. 178.

‡ Solowieff, *Arch. f. path. Anat.* 1875. Bd. lxii. p. 195.

§ Wickham Legg, *Med. Chir. Trans.* 1875. Vol. lviii. p. 345.

Charcot and Gombault have found, within the new connective tissue of the livers of animals whose bile ducts had been tied, a developement of the biliary ducts like that described, first by Waldeyer,[*] and afterwards by Hanot,[†] in hypertrophous cirrhosis. The account is as follows: Under the microscope is seen a large number of winding tubes, often anastomosing and forming a network with irregular meshes. Their number, size, and general direction, vary according to the point looked at; but three zones could sometimes be distinguished in the portal space, more often only two; a central zone filled by large canals; these are not very abundant, and fill the space in the immediate neighbourhood of the vein; they sometimes are prolonged into the fissure, and then fill the middle part; they are in general separated from the other canals by a broad zone of connective tissue. The central zone is the most often wanting. There is also a middle zone in which smaller canals are found than in the first, often anastomosing, but following, as a rule, a direction perpendicular to those of the vessels which radiate from the lobule; lastly, a third zone, formed by very short canals, starting at a right angle from the foregoing to open upon the lobule in a direction parallel to those rows of liver cells with which they seem in certain places to be continuous. These canals are the least in size of all. The contents of the canals are variable. Sometimes they are completely filled with small epithelium cells; sometimes they form on the inner surface an irregular lining, with all the intermediate stages between the cubical epithelium of the fine interlobular canals and the cylindrical epithelium of the larger ducts. When the canal possesses a free cavity, it is sometimes very narrow, sometimes dilated. In the first case the epithelium is large, in the second flattened. Lastly, in the larger canals, the cavity may be obstructed by a mass of pigment.[§] I can attest that these rudimentary biliary ducts are seen in cases of obstruction; for I have recently had the opportunity of verifying Charcot and Gombault's statements in some cases of well-marked cirrhosis from this cause.

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[*] Waldeyer, *Arch. f. path. Anat.* 1868. Bd. xliii. p. 537.

[†] Hanot, *Étude sur une forme de cirrhose hypertrophique du foie*, Paris, 1876.

It is clear that, if the increase of the connective tissue within the liver be at all great, the size of the lobule must decrease; Charcot and Gombault found this really was the case. In the advanced cases the shape of the lobule was much changed, and in a curious way. The lobule is not merely, so to speak, pushed back by the developement of the new connective tissue; in the most wasted of all the lobules the hepatic cells kept shape and size, and even their regular mode of arrangement. They are still seen in rays around the hepatic vein, but at the circumference of the lobule they are stopped abruptly, and each ray differs in length so that the outline of the lobules becomes very irregular. I fear that I am quite unable to corroborate the statements of Charcot and Gombault in this particular. In my own experiments one of the first and most striking results, was the destruction of the natural appearance of the cells arranged in rays around the vein. The cells were

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[*] Charcot and Gombault, *op. cit.* 1876. p. 278.

piled irregularly one on another without any arrangement, and the atrophy of the individual cell was a marked feature in the later cases.

The changes which take place in the cells have been studied by Oskar Wyss,[*] Henrich Mayer,[†] Leyden,[‡] and others. Leyden asserts, basing this statement on the results of the ligature of the bile ducts in more than 20 dogs, that the cells of the liver undergo a fatty infiltration as the chief change. In this he is supported by Hayem and Cornil.[§] The cells in the centre of the acinus were quite as much filled with fat as those in the circumference. It is to be noted that the bile contained fat drops, and the epithelium of the gall bladder and kidney both showed a fatty infiltration. Oskar Wyss, Heinrich Mayer and myself did not find any high degree of fatty infiltration present. In my own cases I found a certain amount of fatty infiltration of the outer zone of the lobule, if death took place a short time after the obstruction was set up: but if later, very little fat was present in the cells; and, on the contrary, the two observers mentioned, and myself, found a wasting of the cells. They became much smaller than in health, they had granular contents and an indistinct looking nucleus, which Heinrich Mayer says is altered, without more specially stating the nature of the change. In several of my cases I have been unable to detect a nucleus, but I think this to be due to some optical defect rather than to a real absence of the nucleus. Charcot and Gombault found a fatty infiltration quite the exception.[‖]

They are unable to state how the liver cell is destroyed. The protoplasm gradually decreases, the cell lessens in size and becomes angular in shape, the contents being homogeneous, shining, and slightly yellow, like glass. The protoplasm does not colour with carmine, but the nucleus does. Charcot and Gombault call this the vitreous degeneration. I have seen this appearance in my experiments, but I do not look upon it as very common.

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[*] Oskar Wyss, *loc. cit.*

[†] Heinrich Mayer, *loc. cit.*

[‡] Leyden, *Beiträge zur Pathologie des Icterus*, Berlin, 1866. p. 83.

[§] Hayem and Cornil, *Comptes rendus des Séances de la Société de Biologie*, Année 1875. p. 309.

[‖] Charcot and Gombault, *Archives de Physiologie*, 1876. p. 281.

Chambard has repeated the experiments of Charcot and Gombault upon guinea pigs and has come to results closely allied to theirs.[*] He has paid special attention to the changes undergone by the cells, and points out the presence of many "transparent spots," as he calls the masses of cells which show the vitreous change described by Charcot and Gombault. Chambard discusses the question if these transparent spots be due to the bursting of a bile duct and the action of the bile upon the cells in the neighbourhood; but rather inclines to the belief that the appearance is caused by the filling of the cells with mucus.

In a few cases of permanent obstruction to the ducts the liver cells have been completely destroyed, just as in acute yellow atrophy, nothing but a granular and fatty detritus being seen under the microscope. This appearance is very rare, and has gained undue prominence from the circumstance that in the very first case in which the liver cells were found dissolved, there was a complete obstruction to the ducts.[†] To explain this solution of the cells, it was thought by Theodor von Dusch that the bile had the property of dissolving the liver cells,[‡] but it has been satisfactorily disproved by Kühne[*] and others,[†] that the liver cell is not dissolved by the bile acids, but that its outline merely is rendered indistinct and faint, but may be readily restored by adding colouring matter to the slide. Oskar Wyss thinks the liver cells in jaundice are more easily destroyed by *post-mortem* decomposition: he says he has been unable to find liver cells from a case of jaundice 48 hours after death.[‡] This cannot be generally true, as I have kept jaundiced livers even in hot weather for 7 days, and yet at the end of that time been able to recognise the cell. Leyden has found that a parenchymatous degeneration of the liver and other glandular and muscular organs follows the poisoning by bile acids.[§] It would be well to keep his observations in mind when seeking for an explanation of the dissolution of the cells, as a parenchymatous degeneration may end in a complete disappearance.

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[*] Ernest Chambard, *Archives de Physiologie*, 1877. p. 718. and *Laboratoire d'Histologie du Collége de France, travaux de l'année* 1877-78, Paris, 1879, p. 31.

[†] Thomas Williams, *Guy's Hospital Reports*, 1843. p. 444.

[‡] Th. von Dusch, *Untersuchungen and Experimente als Beiträg zur Pathogenese des Icterus*, Leipzig, 1854. p. 36.

Frerichs has very fully described the important changes seen in the kidneys. No one before him seems to have paid any attention to their histology in jaundice. As the greater part of the bile pigment leaves the body by the urine, it is natural to expect corresponding changes in the kidneys. After a long-continued jaundice, Frerichs finds the kidneys of an olive green tint; on the surface are seen a few convoluted tubes of a dark colour while in the pyramids, the tubules are brown or green and filled with black deposit. With the microscope, it is seen that the paler tubules are coloured green or brown. The epithelium, rarely completely retained, is coloured deep brown, especially the nucleus. The cells themselves appear some blood red, some green, some brown. Others show layers of pigment arranged in a concentric manner around the nucleus. Epithelium showing marks of fatty degeneration may often be seen of a red, brown, or black colour. When the deposit of pigment has reached its highest degree, the tubules appear filled with a coal black, firm brittle mass. This, like some kinds of black gall stones, resists the action of caustic potash for a long time. Sometimes this deposit of pigment is seen everywhere throughout the kidney, beginning in the Mapighian bodies where it is less marked, and passing through the convoluted tubes till it reaches the straight tubules of the pyramid, which are often plugged with coal-black masses of pigment.*

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[*] Kühne, *Arch. f. path. Anat.* 1858. Vol. xiv. p. 334.

[†] Robin, *Mémoires lus à la Soc. de Biologie*, année 1857. p. 14. See also my own observations, *S. B. H. Reports*, 1873. Vol. ix. p. 180.

[‡] Oskar Wyss, *loc. cit.*

[§] Leyden, *op. cit.* p. 60.

I can endorse these statements of Frerichs; I have seen all that he describes and have very little to add. In some cases there has appeared to me an overgrowth of the connective tissue of the kidney; but this I look upon as an accident, as in a child which had been jaundiced from birth, there was no increase of the connective tissue of the kidney. The striation of the cortex is often perfectly retained in these cases, and the kidney simply looks jaundiced.

Möbius has studied the state of the kidney in jaundice, and endeavours to supplement Frerichs' work on this subject. If a moderate amount of jaundice have lasted a few months, the kidneys will be found of the natural size and consistence, and the surface will be smooth and yellow. No change will be seen in the relation between the pyramids and cortex: this last shows a diffuse yellow colour, which Möbius compares to mustard. The pyramids show dark green stripes, the colour of which is most intense midway between the apex and base. If the jaundice have lasted but a short time the colour is much less marked; while if there have been a complete obstruction to the gall ducts, the cortex is dark yellow ochre, some parts being olive green and the green lines of the pyramids very prominent, becoming in some places black. A scraping of the organ shows under the microscope bright yellow granules of varying size, some free, others in epithelium cells. On hardening the organ, the following appearances can be made out: The glomeruli are entirely free from pigment in all cases: so also is the interstitial tissue; it is only the tubules which show pigment granules, and these are contained in the epithelium of the convoluted tubes, but in greater abundance in the looped tubes. The granules are most common about the nucleus. If the jaundice last long, the inner layer of the capsule is coloured golden yellow, which Möbius thinks is due to the filling of the lymphatic vessels with pigment. The epithelium of the kidney becomes more and more filled with it, and the tubules themselves seem filled with pigment, so as to form casts of tubes formed of bile pigment. Möbius found no pigment in the kidneys in a case of phosphorus poisoning, acute yellow atrophy, or pyæmic jaundice.†

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* Frerichs, *op. cit.* Bd. i. p. 107.

The other glands, the salivary and the pancreas, for example, show but little change. Neither do the sweat glands offer any striking morbid appearance. Frerichs says that now and then the contents of the tubule may appear somewhat yellow, and a few brown pigment granules be seen, but nothing more.‡

The skin as a rule shows after death no change in tint from that in life. If it be examined with the microscope, it is found to show in the lower layers, where the epidermal cells are youngest, the greatest amount of colour. In this it is like Addison's disease. The rounded cells, nearest the true skin, show brown and yellow granules about the nucleus.

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† P. J. Möbius, *Arch. d. Heilkunde*, 1877. Jahrg. xviii. p. 83.

‡ Frerichs, *op. cit.* Bd. i. p. 109.

The mucous membranes which during life show but little of the yellow tinge, become much more coloured after death. Care must be taken in all cases of suspected jaundice not to make any diagnosis from the colour of the conjunctiva after death. This often assumes a distinctly yellow appearance, even where no jaundice or symptom of liver derangement was seen during life.

CHAPTER XIV.

THE FUNCTIONS OF THE LIVER IN JAUNDICE.

BUT little attention has been hitherto paid to the question whether the liver continue its functions in jaundice as in health. Indeed, it seems by some to have been assumed that the functions go on without interruption. The first intimation, since Claude Bernard's discoveries, that such a question was asked may be found in a paper by Kühne on jaundice. Benzoic acid, it is well known, is converted in the body into hippuric acid, probably by combining in the liver with glycocoll, in the presence of bile.* Kühne asserts that if benzoic acid be given to a jaundiced animal, no hippuric acid is seen in the urine, but the benzoic acid appears unaltered. This he thinks due to the liver's functions being altered in jaundice, so that no more free glycocoll or glycocholic acid is formed in the liver, but only taurocholic or cholalic acid.† Kühne's theory, however, was quickly made an end of; for several observers found that the disappearance of the hippuric acid was due rather to the decomposition of urine, and the reappearance of benzoic acid from putrefaction than to any other cause.‡

Golowin was the next, at the suggestion of Botkin, to raise any doubts as to the functions of the liver. From observations on jaundiced men and dogs, he came to the conclusion that the liver at the end of a long-continued jaundice lost the power of secreting bile acids.§ His observations will be spoken of again.

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* Kühne and Hallwachs, *Arch. f. path. Anat.* 1857, Bd. xii. p. 386.

† Kühne, *ibid.* 1858, Bd. xiv. p. 320.

‡ See p. 293 of this work.

§ Golowin, *Arch. f. path. Anat.* 1871, Bd. liii. p. 417.

Skoda looks upon the view that the bile continues to be secreted in continued obstruction as venturesome, and that it is more probable that the pressure in the ducts causes a hindrance to the secretion of the cells. He even goes so far as to think that jaundice may be absent in complete obstruction to the ducts. Jaundice may decrease even if no bile pass into the intestine.* Very similar views are expressed by Jaccoud.†

The disturbing influence of jaundice upon the several functions of the liver will now be considered, each function being taken by itself.

i. The most important function of the liver known to us at the present day is the preparation of glycogen. This appeared to me so important a point to establish on a firm basis, that I have made a large number of observations upon animals in order to decide this point. In all cases I found that whether the animal died within a few hours or a few days after ligature of the bile ducts, in all cases alike, glycogen was absent from the liver. Glycogen was absent in all cases; it is not, therefore, merely the outcome of temporary disturbance due to the changes set up by the wound and other circumstances, but a permanent change in the function of the liver. The glycogen in no case returned again.‡ These observations have been confirmed by von Wittich,§ E. Külz, and E. Frerichs.‖ In like manner, puncture of the fourth ventricle failed to cause sugar to be present in the urine a few days after ligature of the common duct.¶ It is evident, therefore, that in complete obstruction of the ducts the liver ceases to prepare glycogen.

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* Skoda, Virchow and Hirsch's *Jahresbericht f.* 1868, Bd. ii. p. 142.

† Jaccoud, *Leçons de clinique méd.* (Lariboisière), Paris, 1873, p. 545.

‡ Wickham Legg, *S. Bartholomew's Hospital Reports*, 1873, Vol. ix. p. 161.

§ Von Wittich, *Centralblatt f. d. med. Wiss.* 1875. p. 291.

‖ E. Külz and E. Frerichs, *Arch. f. d. ges. Phys.* 1876. Bd. xiii. p. 460.

¶ Wickham Legg, *Arch. f. exp. Path.* 1874. Bd. ii. p. 384.

It becomes a question now how far this fact in animals may be applied to jaundice in men, when there is sometimes evidence, from the presence of colour in the stools, that the obstruction to the ducts is not complete. In these and other cases, the phænomena seem best explained by supposing that the glycogenetic function of the liver is not altogether abolished, but rather impaired. Even in cases of simple jaundice the patient wastes and loses flesh rapidly, and this seems best explained by supposing a great impairment, if not destruction, of the glycogenetic function. Glycogen is always found in growing parts, and its importance to nutrition cannot be doubted.

The like absence of glycogen and sugar in the liver was found by Küthe in dogs in whom a biliary fistula had been established. The wasting which follows the setting-up of this flux is well-known.[*]

There is a case of Dr. Bright's, often quoted, of the concurrence of jaundice and diabetes. It is highly interesting. A man aged 49, of sober habits, became diabetic in March, 1827. At the beginning of September he became jaundiced, and by the end of December, the diabetes had disappeared. He died on March 1st, and the cause of death was found in a tumour of the pancreas, in which the dilated bile ducts terminated in a *cul de sac*.[†] Here the diabetes continued until it was put an end to by a permanent obstruction of the bile ducts.

ii. There is a second function of the liver, the secretion of bile. Now the important constituents of the bile are the pigment, the bile acids, and cholestearin. The amount of bile excreted by a healthy man has been very variously estimated. Let us take 10 grammes, the estimation of Westphalen,[‡] so that the following figures may be within the bounds of probability. Of these 10 grammes of dry bile, 5 must be made up of the soda salts of the bile acids, about one by mucus and pigment, and the remainder by cholestearin and the inorganic residues. Now if the liver in jaundice continue its functions of bile-making uninjured, there ought to pass out of the system daily, amounts of bile pigment and bile acids equivalent to these. The only secretion which has been hitherto found to contain them is the urine; and the urine therefore is to be examined with this view.

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[*] Küthe, *Zur Function der Leber*, in Heynsius' *Stud. d. phys. Inst. zu Amsterdam*, Leipzig and Heidelberg, 1861. p. 52.

[†] Bright, *Med. Chir. Trans.* 1833. Vol. xviii. p. 3.

[‡] See p. 105 of this work.

First as to the bile pigments. The urine is often deeply coloured, and its appearance would almost justify the belief that the same amount of the bile pigments which in health is passed into the duodenum must be contained in the urine. Yet Schwanda in his estimations found surprisingly little pigment. In the highest, the amount was only ·015 grm. in the twenty-four hours. In others, ·014, ·012, ·011, ·005, and even ·002, that is, only 2 milligrammes.[*] Thus the amount of pigment excreted by the urine is infinitely little when compared to the amount of pigment excreted by the liver in health. What is the reason of this difference? To me the best answer to this question seems to be that in jaundice the pigment-forming function of the liver is much injured. I am aware of the difficulties which this solution itself raises, but at present this theory seems to me best to explain facts.

Then as to the bile acids. The part which these play in the phænomena of jaundice has for some years past been a *crux* to pathologists. Formerly they could not be found in the urine, and there was great strife as to the cause of their absence. Now all agree that the bile acids are present in the urine; but they are present in very small quantity. At the reckoning given above the liver ought daily to secrete at least five grammes of the bile acids. Now in jaundice, if we may believe what the chemists tell us, not so much as half a gramme passes out of the body daily by the urine. If the whole of the natural amount of the bile acids be secreted, what becomes of the remaining four and a half grammes? Ernst Bischoff, in answer to this question, imagines that the blood has the power of burning off so much of the bile acids, and no more; that in jaundice more bile acids are taken into the blood than can be destroyed there, and that then the unconsumed excess is excreted by the kidneys.[*] He thinks there are only two hypotheses; one, that the bile acids cannot be destroyed in the blood, and so do not pass into it in health; or that in jaundice more bile passes into the blood than can be consumed therein. He hardly contemplates the possibility of the bile acids ceasing to be secreted in jaundice; in fact he brings forward some reasoning and experiments which seem to show that all the sulphur of the bile acids which should be excreted *per anum*, passes out in jaundice through the urine.[†]

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[*] Schwanda, *Wien. med. Wochenschrift*, 1865. p. 989. See above, p. 30. for the observations of Städeler on the great colouring powers of the bile pigment. A solution of one in a million was distinctly yellow in a two-inch layer.

Leyden criticises Ernst Bischoff's theory by noting that even in slight cases of jaundice the bile acids may be found in the urine. If any quantity of the bile acids were burnt off in the blood, there would in such cases be no excess to appear in the urine. Also if bile acids be injected under the skin of rabbits, they make their appearance in the urine, and the absorption is certainly very slow. And in these cases and in jaundice it is a long time before the bile acids entirely disappear from the urine. But it is very important that the resistance of the bile acids to chemical action should be borne in mind. They do not readily decompose even when added to putrid urine.[*]

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[*] Ernst Bischoff, *Zeitschrift f. rat. Med.* 1864. iii. Reihe, Bd. xxi. p. 144.

[†] He reasons thus: dry bile contains from ·83 to 2·99 *per cent.* of sulphur: the mean is 1·5 *per cent.* Now taking 17 grm. as the amount of dry bile daily passing down the common duct (a low estimation) ·3 grm. of sulphur are daily excreted. But the fæces do not contain all this sulphur, part is absorbed and probably passes out in the urine: the amount of sulphur passed in health by stool is only ·26 grm. Now in jaundice there is exactly ·26 grm. of sulphur in the urine more than in health. Bischoff seems to suggest that the taurocholic acid is the source of this extra sulphur. (*op. cit.* p. 147.) This reasoning is open to many objections. It has been criticized by Leyden. (*op. cit* p. 37.)

There is, moreover, an objection at first sight to believing that the secretion of bile is unaltered in jaundice: it seems hardly likely that when the excretory duct of a gland is obstructed, the secretion into that duct should continue unchecked. Again Schiff thinks that a kind of circulation of bile between the liver and intestine goes on, and that when the supply of bile is cut off from the intestine, the amount of bile becomes much less.[†] Further, H. Huppert found that when the bile acids are injected into the blood, a considerable excess of bile acids is excreted by the liver in the bile.[‡] It is thus possible that in jaundice the secretion of bile acids is much lessened, as no supply is drawn from the intestines, the gall duct being blocked up. Looking therefore at these facts just mentioned, the undoubted smallness of the amount of bile acids in the urine of jaundice and the intimate connexion between the bile-making function and the glycogenetic function,[§] it would seem the most probable theory that in jaundice very little of the bile acids is secreted; and that, when the jaundice is of long standing, and the glycogenetic function completely abolished, the bile acids likewise cease to be secreted, as the observations of Golowin and others teach.*

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[*] Leyden, *Beiträge zur Pathologie des Icterus*, Berlin, 1866. p. 40.

[†] Schiff, *Arch. f. d. ges. Phys.* 1870. Bd. iii. p. 598.

[‡] H. Huppert, *Arch. d. Heilkunde*, 1864, p. 244.

[§] That there is an intimate connexion between the two can scarcely be doubted. Bernard found in the *Limax* that the liver alternately secreted bile and sugar. (*Leçons sur les propriétés physiologiques et les altérations pathologiques des liquides de l'organisme*, Paris, 1859. t. ii. p. 203.) It is probable also that albuminous matters are broken up in the liver, the carbon, hydrogen, and oxygen, going to form glycogen, while the refuse of this process, the carbon, hydrogen, oxygen, sulphur and nitrogen, forms the bile acids.

What is now wanted are more and accurate estimations of the amount of bile acids passed in the urine of jaundice. Some may doubt if the amount of bile acids have ever been accurately estimated; but there is no good reason for denying that the amount is very small; and the quantity given above, half a gramme, is far higher than that given by any observer who has estimated them.

It may well be asked: why, if the secretion of bile be entirely stopped, do the skin and urine become so coloured? To this it may be answered: it is not affirmed that the secretion of bile is entirely suppressed; witness the presence of the bile acids and bile pigment in the urine, though in small quantity; and if a small quantity of bile pigment only be secreted, it would be enough to colour the skin and urine. The yellow colour which is common in jaundice is indeed an argument in favour of the secretion being suppressed; for if the whole amount of pigment, natural in health, continued to be secreted, the skin of every jaundiced European would resemble a negro. That there is a decrease of the amount of pigment is attested by Dr. Budd who says: "It sometimes happens that after complete closure of the common duct has existed many months, and while no bile flows through it into the intestine, the jaundice of the skin becomes very much less deep, and the urine very much less deeply stained with bile. I have, indeed, more than once known the jaundice gradually diminish and almost entirely disappear after the lapse of twelve months, to the great satisfaction of the patient, although the colour of the intestinal discharges and an examination of the body after death, showed that the closure of the duct was still complete."[*] Dr. Murchison has some remarks to the same effect.[†]

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* See the section on the urine, p. 286 of this work.

iii. A third important function of the liver is the maintenance of animal heat. For the discovery of this important office we are again indebted to Claude Bernard. He found that the temperature of the blood coming from the hepatic veins was higher than that of any other part of the body.[‡] The high temperature is clearly due to the active chemical processes which go on in the liver, the oxydations connected with the formation of glycogen, of bile, and with the process of sanguification. If the arguments used in the foregoing paragraphs be at all sound, it should follow that, in obstruction to the ducts of the liver, and consequent abolition of two important functions, the temperature of this organ should fall, and with it the temperature of the whole of the body. It is notorious that the temperature in jaundice is almost always below the natural standard; and that even in those cases where a pyrexial complication is present, the temperature never rises so high as is customary in uncomplicated disorders.

While passing through Lyons after the Easter of 1878 I had an opportunity, thanks to the courtesy of M. Chauveau, of making some experiments directed to this point. The bile ducts of dogs were ligatured, and forty-eight hours after the ligature of the ducts, the temperature in the upper part of the inferior cava was ascertained, by means of a thermometer passed through the jugular and right auricle. It was found, however, that a traumatic pyrexia had been set up, and the temperature of the vena cava and of the rectum was in all cases equal. It would be necessary, in any other series of experiments, to wait until the pyrexia had gone down. This, again, involves a risk, as the animals are not likely to survive the operation many days.

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[*] Budd, *On Diseases of the Liver*, London, 1857. p. 231.

[†] Murchison, *Clinical Lectures on Diseases of the Liver*, London, 1868. p. 427.

[‡] Bernard, *Leçons sur les propriétés physiologiques et les altérations pathologiques des liquides de l'organisme*, Paris, 1859. t. i. p. 85.

iv. There is said to be another function of the liver, to which allusion has already been made; that of sanguification. C. G. Lehmann found the blood of the hepatic vein to contain a far greater number of red and colourless corpuscles than that of the portal vein. The number of the colourless corpuscles is also increased relatively to the red. The red are distinctly violet in colour, and they resist the action of water upon them.[*] He also says that the red corpuscles are smaller, and less regularly lenticular.[†] The blood of the portal vein also shows fibrin in no way different from that of the rest of the body: but the blood from the hepatic vein can hardly be got to clot at all, and when whipped, shows only a few threads of fibrin. The extractives and fats are also in greater quantity in the hepatic vein than in the portal.[‡]

Ernst Hirt confirms Lehmann's statement as to the increase of the white corpuscles; he finds that the number of white corpuscles to the red in the blood of the portal vein is about 1 to 700 or 750, while in the hepatic vein the number is about 1 in 68 or 274.[§]

Dr. McDonnell, so well known from the numerous observations which he has made on the functions of the liver, affirms without hesitation that the blood of the hepatic veins of dogs is not capable of coagulating spontaneously, and that it does not give fibrin on being whipped, and that the hepatic blood contains colourless corpuscles five to ten times more numerous than in the portal blood.[*]

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[*] C. G. Lehmann, *Physiological Chemistry*, Cavendish Soc. ed. Vol. ii. p. 259.

[†] Idem, *Journal de Pharmacie et de Chimie*, 1852. t. xxi. p. 396.

[‡] Idem, *Comptes rendus*, 1855. t. xl. p. 585. The absence of coagulation in the blood of the hepatic vein has also been noted by Brown-Séquard. (*Journal de la Physiologie*, 1858. t. i. p. 298.)

[§] Ernst Hirt, Müller's *Archiv. f. Anat. Phys.* 1856. p. 191.

Flügge, comparing analyses of the blood of the portal and hepatic vein, has come to the conclusion that there is but little difference between the blood in these two vessels. He found the amount of the solids, nitrogen, phosphates, and chlorides, almost the same in both, and the amount of hæmoglobin about equal. So that if Flügge's observations and his method may be trusted, great doubts will be thrown upon the functions of the liver as a blood-making organ.[†]

Drosdoff, however, has made analyses of the blood of the portal and hepatic veins in Hoppe-Seyler's laboratory in Strassburg, and sharply criticises Flügge's methods. Drosdoff finds that the solids of the portal vein are always greater than those of the hepatic, and that the hepatic vein is always richer in cholestearin and lecithin than the portal vein, while the reverse holds good about fats.[‡]

There are many analyses and observations which show that in jaundice the amount of red corpuscles is much decreased.[§] Budd attributes this not so much to the mere presence of the principles of the bile in the blood, as to the diminution of those reparative changes which the blood naturally undergoes in its passage through the liver, and on the absence of bile in the intestines.[||] I feel disposed to agree with Budd rather than with Leyden, who thinks that the poorness of the blood is due to the action of the bile acids upon the blood corpuscles.[¶] For if, as in the foregoing paragraph upon the secretion of the bile I have endeavoured to show, the whole amount of bile acids poured into the circulation daily be less than half a gramme, the action of the bile acids upon the corpuscles must be extremely small, since the bile acids will be in so dilute a solution that they can scarcely be thought to act on the corpuscles.

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[*] McDonnell, *Observations on the functions of the Liver*, Dublin, 1865. pp. 28 and 38.

[†] Flügge, *Zeitschrift f. Biologie*, 1877. Bd. xiii. p. 133.

[‡] W. Drosdoff, *Zeitschrift f. phys. Chemie*, 1877. Bd. i. p. 233.

[§] See the section on the blood in jaundice, p. 269.

[||] Budd, *On Diseases of the Liver*, London, 1857. Third Edition, p. 468.

[¶] Leyden, *Beiträge zur Pathologie des Icterus*, Berlin, 1866. p. 118.

CHAPTER XV.

THE DIAGNOSIS AND PROGNOSIS OF JAUNDICE.

Diagnosis. The diagnosis of jaundice is commonly a matter of extreme ease. All that is necessary is to look at the patient's face, and especially the conjunctiva, by daylight. To confirm this observation it is often desirable to ascertain the presence of bile pigment in the urine, and the absence of colour in the fæces.

There is one discoloration of the face very liable at a superficial glance to be mistaken for jaundice, and that is the yellowness caused by exposure to the sun. It is seen, of course, chiefly in men, but the conjunctivæ remain colourless, and the urine free from bile pigment. Further, the parts covered by clothing are of the natural white.

The same pearly whiteness of the conjunctiva, and absence of the bile pigment from the urine distinguish chlorosis, in which the skin is often of a yellowish tinge, the cachexia of cancer, lead poisoning, and agues. It seems unlikely that the pigmentation of the skin in Addison's disease should be mistaken for jaundice; and some assert that the yellowness of the new-born is shown not to be a jaundice by the absence of colour from the conjunctivæ and of bile pigment from the urine.

In some persons a layer of fat lies immediately under the conjunctiva, and it is necessary to add a caution to the young practitioner, not to be deceived by this, as it causes a yellow appearance liable to be mistaken for slight jaundice. It will be known because the yellow colour is not present everywhere in the conjunctiva, but only in those parts of the sclerotic where the fat is most abundant.

Jaundice may be feigned by soldiers, sailors, and prisoners, for their own purposes. It is done by staining the skin with any yellow pigment: infusions of saffron, turmeric, and the like are said to be those most commonly employed. Such deception may be easily detected, as the conjunctivæ remained uncoloured; and a little soap and water, or chlorine water, or chloride of lime, will discharge the colour of the skin. If their cunning have gone the length of taking rhubarb or santonin for the purpose of darkening the urine, the urine will be deepened to a red by alkalies, whereas the urine of true jaundice is coloured brown. Further, there will be no reaction with nitric acid.

A far better means for deceiving the physician would be the carbazotate or picrate of potash taken internally. This is said to stain the skin and tissues of a fine yellow, but the urine does not contain bile pigment, nor are the stools colourless.

Nothing can be easier than to say that a patient is jaundiced; but it is often one of the most difficult problems in medicine to point out the cause of the jaundice. It is sometimes hard even to approach a diagnosis, nothing but a guess being possible; and it is not often that the physician can feel very great confidence in the opinion which he puts forth. A few suggestions are added upon the lines of which the clinical physician may work in his search after the causes of jaundice.

First, it is of considerable importance to be able to feel the distended gall-bladder at the lower border of the right lobe. If this can be distinctly felt and percussed out, much information is gained. The cause of the jaundice will in all likelihood be below the junction of the cystic and hepatic ducts, in fact, in the common duct. In cases where the jaundice is due to changes in the liver itself the gall-bladder is very often empty or only half filled, and cannot therefore be felt.

Next, the state of the stools must be looked into, whether they be altogether or but partly free from colour. It may be thought by some that a complete absence of colour in the stools is a sign of complete obstruction of the duct.

i. Should the jaundice be recent and no perceptible disease be found in the liver or elsewhere, the case is probably one of simple jaundice.

ii. The jaundice being recent but acute disease of other parts present: such as pneumonia, pyæmia, typhoid and relapsing fevers, and the like, delirium tremens, poisoning by chloroform, chloral hydrate and other drugs, and snake-bites, the cause of the jaundice is not known with any certainty; but it is probably the same as in simple jaundice.

iii. If the jaundice be accompanied or preceded by attacks of severe shooting pains in the right hypochondrium; or if the jaundice be intermittent, one attack quickly succeeding the other, the cause is probably gall-stones.

iv. An intense persistent jaundice, if approaching twelve months in duration, is due, probably not to cancer, but to gall-stones, hydatids, or stricture of the duct.

v. A slight persistent jaundice is probably due to changes in the texture of the liver, as cirrhosis, nutmeg liver, &c.

vi. Jaundice with great enlargement of the liver is probably due to cancer.

vii. Jaundice complicated with ascites is probably due to cirrhosis.

viii. Delirium setting in during an acute jaundice suggests *icterus gravis*.

Prognosis. The length of time which a jaundice may last varies with the cause of the jaundice. In one case, the yellowness may be a mere transitory symptom, lasting but a few days, the conjunctiva only being coloured, and the urine just showing a faint reaction of bile pigment. In another, the jaundice may be intense and last three or four years. Or the patient may recover from one attack, only on recovery to fall into another access of the same disease, and this alternation of health and disease may last many months, or even years. Such a case is reported by Van Swieten, in which a woman had jaundice off and on for 12 years.* Heberden says he has known the jaundice return frequently for more than 20 years in some persons, who have had good health in the intervals of the fits. He also speaks of a woman who for five years laboured under all the usual symptoms of the jaundice in the highest degree.† Dr. Joseph Ayre speaks of a gentleman who had been jaundiced for eight years from a permanent obstruction of the biliary duct,‡ and Devay of a woman who stated that she had been jaundiced for 7 years.§ She was only under observation a few days before death; a peasant, and of "*intelligence faible et grossière*," so that but little trust can be placed in her statements. I have myself seen a patient jaundiced continuously for six years and a half, and yet able to do light work, such as book-keeping or account keeping.

How long may a patient live with the gall ducts completely obstructed? Graves and Stokes have recorded a case of jaundice in which the stools were colourless for two years, yet the appetite returned, the bowels became regular, and all bad symptoms disappeared.‖ Dr. Hilton Fagge speaks of a case lasting 7 years with persistent jaundice.* But there is every reason to think that a case of complete obstruction to the gall ducts rarely lasts for more than a twelve-month. Very few of my own cases have lasted so long. The matter is of course different when the obstruction is incomplete, or the jaundice intermitting.† Much also, in the length of time which jaundice will last, depends upon the nature of the obstruction. Jaundice caused by cancer will, in the usual course of events, end more quickly than that caused by hydatids, gall stones, or other permanent constriction of the duct.

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* Van Swieten, *Comment.* § 950, Lugd. Batav. 1755, t. iii. p. 130. This case is usually quoted as if the jaundice had persisted for 12 years without intermission. It was continuous only for the last of the twelve years.

† Heberden, *Commentaries*, Lond. 1806, Third ed. p. 243.

‡ Joseph Ayre, *Practical Observations on those Diseases of the Liver, etc.* Lond 1821, p. 16.

§ Devay, *Gaz. méd. de Paris*, 1843, p. 263.

‖ Graves and Stokes, *Dublin Hospital Reports*, 1830. Vol. v. p. 109.

The prognosis of jaundice depends solely on the cause. If due to organic disease of the liver, the prognosis becomes involved in the liver disease. If, as in so many cases of simple jaundice, there be no apparent disease of the liver, the prognosis becomes exceedingly favourable; the immense majority of cases of simple jaundice end in six weeks in the complete recovery of health. Still, the practitioner can never feel quite happy even when attending the simplest case of jaundice, as the beginnings of acute yellow atrophy cannot in the present state of knowledge be distinguished from simple jaundice. The physician should thus be on his guard not to give too confident a prognosis, lest in a few days delirium or coma come on, and his forecast falsified.

The appearance of nervous symptoms or of hæmorrhages, whether in acute or chronic jaundice, is certainly of very evil augury, and is most commonly the forerunner of death. The same may be said of a rise of temperature. The slow pulse is usually without influence on the prognosis; Karl Kétli has, however, published a case of jaundice in which death seemed to take place from the heart; the pulse became slower and slower, until the patient died.* Itching and xanthelasma have no influence on the prognosis. Xanthopsy and nyctalopia are thought by some to be very bad signs.

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* Hilton Fagge, *Guy's Hospital Reports*, 1875. Vol. xx. Third series, p. 164.

† Hertz has published (*Berlin. klin. Wochenschrift*, 1877, p. 76) a case with details rather obscurely related in which the same intermitting jaundice was noticed from Christmas, 1871 to death in April, 1874. It would seem, but this is not at all clear, that the jaundice was persistent the last two years before death.

The best symptom that can be seen in jaundice is a return of colour in the stools. This symptom appears first of all, long before the yellow colour has begun to disappear from the conjunctiva, or the urine to lose its pigment: indeed the urine, as it is the first to show the pigment, so it is often the last to lose it. Care must be taken in judging of the stools to be sure that the colour is due to bile, and not to a foreign admixture.

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* Karl Kétli, *Wien. med. Wochenschrift*, 1878. p. 135.

CHAPTER XVI.

THE TREATMENT OF JAUNDICE.

JAUNDICE is but a symptom; and in its treatment, attention must be first of all paid to the causes which bring about the jaundice. If the jaundice be associated with a gastro-duodenal catarrh, this state of the mucous membrane must first be remedied. If the jaundice be due to the pressure upon the gall duct of hardened fæces in the large intestine, these should be removed. Or if due to the passage of gall stones, the main aim of the physician will be to render the escape of the gall stone from the common duct more easy. If tumours outside the liver, and these may spring from any neighbouring organ, press on the gall ducts, an attempt should be made to relieve the pressure. In jaundice from disease of the liver, the disease of the liver itself should be treated, and the jaundice may almost be neglected. Thus the treatment of jaundice resolves itself into the treatment of the disease causing the jaundice, and to this the judicious practitioner will commonly restrict himself.

But though the treatment of jaundice should be left to that of the disease by which it is caused, yet the results of the jaundice, the injuries done to the functions of the liver, and the consequent damage to the general health, deserve some attention. The means at our disposal for the relief of these states are but feeble, as it would be folly to expect that the effect would cease while the cause is in active operation.

First, the supposed injury to the digestion in the intestines from the lack of bile may be considered. It is doubtful, however, if bile be of any importance, save for the digestion of the fats; and seeing this, fat should be carefully excluded from the diet of the patient, if he do not instinctively shun it. To remedy the want of bile in the intestine, it was proposed many years ago by Eaglesfield Smith to give the bile of animals to patients suffering from jaundice,[*] and in the present day, ox-bile is given, enclosed in capsules, nicely regulated, it is said, to break at the moment of passing the pylorus. Setting aside the question whether they do indeed melt at the right moment, or whether they do not beforehand discharge their contents in the stomach, and thus upset the process of gastric digestion, experience does not give a very favourable account of their method. I have seen the capsules employed, and I do not think I have noted any marked benefit follow their use. Indeed, it was hardly to be looked for.

Secondly, the damage done to the liver itself. Physiologists are not acquainted with any means for artificially supplying glycogen; nor do therapeutists know any remedy by which the overgrowth of connective tissue in the liver may be checked. But some attempt may be made to stay the wasting and anæmia which are associated with the hindrance to the flow of bile into the duodenum. Attention to the nutrition of the patient formed a large part of the treatment of Hippocrates.[†] Fatty foods, it has been said, are improper; and thus cod-liver oil should be excluded. Nitrogenous aliments should be chiefly used; such as lean beef or mutton. Some writers represent patients with jaundice as suffering from much flatulence; and when this is the case, it would certainly be proper to abstain from food containing starch and sugar. If no inconvenience be felt from wind, this kind of food would be desirable, when the direct supply of fat is taken away.

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[*] See above, p. 135.

[†] Hippocrates, *de locis in homine*, Cap. xxviii. Littré's ed. t. vi. p. 320.

The impoverishment of the blood should be met by giving some of the neutral preparations of iron, such as the reduced iron; or the old steel wine, prepared from iron filings; or Squire's chloroxyde. Sometimes the patient may with benefit be sent to a chalybeate spring; advice given by Sydenham two hundred years ago.[*]

It has been already stated that the great channel by which the bile pigment and bile acids leave the blood is the urine. By the skin only a very small amount is excreted; by the other glands, nothing. In many cases of jaundice, the amount of urine is much increased, and it is desirable to keep up an increased flow of urine, a plain indication of nature, by means of drugs.[†] The neutral salts of potash and soda, especially the citrates and acetates, will be found useful, aided by the mineral waters commonly used as drinks, such as Seltzer, or Apollinaris. Frerichs recommends lemon juice, one and a half to three ounces daily, and says it has the advantage of both aiding digestion and causing an abundant diuresis.[‡]

The activity of the skin should be favoured by warm clothes and warm rooms, especially as the temperature of the body is often low. Of the action of Turkish baths in jaundice I have unfortunately no experience. They are likely to further the excretion of the colouring matters by the skin, and at the end of the disease to favour the disappearance of the yellow colour. It is, when the obstruction to the ducts has been removed, that the skin and kidneys may most advantageously be stimulated; and at the same time excretion of bile may be increased by doses of the alkaline benzoates.[§]

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[*] Sydenham, *Processus Integri*, Cap. xxix. in *Opera omnia*, ed. Greenhill, p. 583.

[†] Warm baths and diuretics formed great part of the Hippocratic treatment of jaundice. (*Op. cit.* pp. 244 and 320.) Graves hints rather obscurely at the use of diuretics. (*Clinical Lectures*, Dublin, 1864. p. 633.)

[‡] Frerichs, *Klinik d. Leberkrankheiten*, Braunschweig, 1858. Bd. i. p. 129.

[§] Benzoic acid was recommended by C. Ph. Falck of Marburg in cases of

These salts are said to rapidly clear the skin of colouring matters.

Besides the rational treatment of jaundice, there are other, empirical methods, which have been employed from the earliest times, and of which it is now necessary to speak. Amongst these stand purgatives and emetics, acids and alkalies, and substances supposed to have a direct action on the liver, such as the juice of certain plants. Some of these empirical methods of treatment are identical with those which we call rational.

i. Purgatives have long enjoyed a great reputation. Calomel used formerly to be given in all cases of jaundice, and physicians were not content with giving it merely as a purgative occasionally, but it was almost a routine practice to give mercury so as to affect the mouth, and to bring on salivation. This has doubtless caused it to lose its reputation, as well as the evidence lately offered that it has no specific action on the flow of bile into the intestine. Podophyllin, which is called the vegetable mercury, has, it is said, a more active influence upon the secretion of bile; but for this very reason it seems to me undesirable to be used in cases of obstruction to the ducts, or disease of the liver.*

Other purgatives, besides mercury and podophyllin, were used, such as jalap and cream of tartar, sulphate of magnesia, aloes, and colocynth. Or the patient was sent to drink the purging waters at Harrowgate, Cheltenham, Friedrichshall or Püllna. I should, however, long hesitate before I subjected a patient with a chronic jaundice to a course of purgative

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jaundice and liver disease. (*Corr. Bltt. d. Ver. f. gemeinsch. Arb.* No. 30. reported in Canstatt's *Jahresbericht f.* 1858. Bd. v. p. 126.) Justi used it with good success in the jaundice of children (*ibid.* No. 31.) but it should be remembered that the jaundice of children usually runs a very favourable course.

* See the chapter on the Action of Drugs upon the Secretion of the Bile, pp. 157, 174 and 178.

medicines. One purgative dose may be given early in the treatment, or perhaps when the bowels become costive; but a series of purgings will lower the patient's strength, or even do him a serious damage.

ii. Emetics were once greatly in vogue for the cure of the jaundice.* By the act of vomiting, the liver and gall-bladder are pressed upon from three sides, and it was thus thought that the bile would be forced out into the duodenum through any moderate obstruction. This may possibly be the case if the obstruction be nothing but a plug of mucus; for it may be seen after death how slight a pressure on the gall bladder will suffice to send the bile into the duodenum. Still, the diagnosis must have attained a high degree of certainty for such violent remedies as emetics to be indicated; for, if the obstruction be a solid tumour pressing on the ducts, or a cancerous head of the pancreas, or a large gall stone firmly impacted in the ducts, an emetic is more likely to cause a rupture of the gall bladder or ducts than a resolution of the obstruction.

If the foregoing be a correct account of the action of emetics in jaundice, it is clear that they are worse than useless in all cases of jaundice from disease of the liver or where the obstruction in the large ducts is of a permanent kind. The cases in which emetics may be most serviceable are those of jaundice caused by a plug of mucus, or a small easily-moved gall stone.

The tartar emetic has been much lauded. Frerichs says that he found the bile passages of dogs to whom he had given tartar emetic empty and perfectly free from bile.† Still tartar emetic cannot be recommended in cases of acute catarrh of the stomach. It is well known that antimony and its congeners cause a catarrh and fatty degeneration of the tubular glands of the stomach: and it would seem unwise to prescribe a drug which has the power of begetting the same disease as that from which the patient already suffers. Ipecacuanha has also been recommended, and if emetics be determined upon it would seem preferable to antimony. Sir Dominic Corrigan recommends it in 30 grain doses every other day.*

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* Hippocrates recommends them. (*De affect. inter.* Cap. xxxv. Littré's ed. t. vii. p. 254.)

† Frerichs, *op. cit.* Bd. i. p. 131.

It would need much stronger evidence as to the value of emetics in jaundice than at present exists, to persuade me to recommend a course of such treatment to a patient suffering even from simple jaundice.†

iii. Acids, both mineral and vegetable, have long enjoyed a great reputation in the treatment of jaundice; and they may be used without fear of any of the ill effects which sometimes accompany emetics and purgatives. Heberden says he has known large quantities of acid, such as lemon juice, gain the credit of the cure of jaundice;‡ and Scott praises the nitro-muriatic acid given by the mouth or used in the bath.§ For this latter purpose I can hardly recommend it; but I think I have seen good follow doses of ten or twenty minims of the dilute acid three times a-day. The action of the acid is explained in different ways. Some think that *aqua regia* has a specific action upon the liver, and appeal to Dr. Rutherford's observation: others think that acids act by irritating the duodenal papilla as in Claude Bernard's well-known experiment.||

iv. The alkaline carbonates and soaps were formerly given, to make amends for the deficiency of the bile, by aiding the digestion and cleansing the bowels.¶ At the

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* Corrigan, *Dublin Hosp. Gaz.* 1845, pp. 69 and 71.

† Stoll condemns the use of emetics in jaundice and says he has seen much harm from them. (*Rat. Med.* pars iii. Viennæ, 1780, p. 388.)

‡ Heberden, *Commentaries*, London, 1806, Third ed. p. 259.

§ H. Scott, *Med. Chir. Trans.* 1817, Vol. viii. p. 173.

|| See pp. 127 and 173 of this work.

¶ Heberden, *loc. cit.*

present day they are most commonly administered in the Carlsbad and Marienbad waters. With these, it must be remembered, a large amount of water is taken, as well as other salts besides carbonates, but they sometimes relieve cases in which other remedies had been unsuccessful.

In the early stages of a jaundice complicated with gastric catarrh, a mild alkaline course is often most useful.

v. Simples have enjoyed a great reputation, the foundation of which is thought to have been laid by Van Swieten. He treated a woman, 60 years old, who had been troubled with the jaundice for 12 years, after the following plan: the juice of grass, milk whey, and the like during the spring; the Spa waters during the summer; and Venice soap and honey during the winter. For six months she had a cœliac flux, and passed abundance of small stones, with recovery.[*] In like manner the juice of the *taraxacum* and of the *carduus benedictus*, especially if freshly expressed, has been much lauded, chiefly by village practitioners.[†] There is, however, very little evidence of the value of these herbs in the treatment of jaundice.

Conium, belladonna, and other anti-spasmodics, were much used in the treatment of jaundice when it was thought that the symptom depended on spasm of the gall ducts; and with the revival of a doctrine of *icterus spasticus* may come again into fashion.

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[*] G. van Swieten, *Comment.* § 950. Lugd. Batav. 1755, t. iii. p. 130.

[†] Some of the remedies for the jaundice used by the public, and which have in a few instances made their way into pseudo-therapeutic works, are more interesting to the student of folk lore than to the physician. Such are the administration of spiders and lice; the mixing of urine with honey and sugar; (Cf. Pliny, *Nat. Hist.* Lib. xxx. Cap. xi.) making a cake with the urine of the patient and meal, and giving it to a dog, who must be of the male sex; or the more loathsome suggestion of dosing the patient with the excrements of the goose; a plan of treatment which I believe the homœopathists have made their own, and in the possession of which no one is likely to disturb them.

With Bamberger,* we may regret that not a step has been made forward in the treatment of jaundice for 2000 years, and that the therapeutics of this age are, in all essential points, the same as those of Hippocrates and the early Greeks.

Treatment of the Complications of Jaundice. The wasting has already been spoken of. The patients are often chilly, and complain of a sensation of cold: this may best be treated by attention to the clothing, which should be a matter of care in nearly all cases of jaundice. The high temperature which comes on just before the fatal ending of the case should not, in my opinion, be treated.

The itching of the skin is sometimes so severe that narcotics must be given to procure sleep. I have myself seen the most relief from mercurial ointments, made with calomel or white precipitate. Sometimes spirituous lotions, containing hydrocyanic acid, or carbolic acid and glycerine, give ease. The warm bath with friction may also be employed.

The slow pulse and changes in the senses do not need special treatment.

The setting in of hæmorrhages is of bad omen, and little can be done by way of treatment.

Gallic acid and tannic acid may be used internally and externally; or large doses of the tincture of iron, or turpentine may be given. If the bleeding be from the nose, and very abundant, it would be right to plug the nares.

Like the hæmorrhages, the appearance of nervous symptoms is a bad sign. I have seen advantage in these cases from active purging; but severe treatment such as blisters to the head or nape of the neck, leeches, hourly doses of calomel, and the like, cannot be recommended.

The xanthelasma should remain untreated.

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* Bamberger, *Krankheiten des chylopoët. Systems*, Erlangen, 1864, p. 484.

CHAPTER XVII.

ICTERUS SIMPLEX.

SYNONYMS. *Icterus communis, benignus, catarrhalis, gastroduodenalis, duodenalis, spasmodicus, spasticus, vernalis.*

Simple jaundice is a mild disorder which runs a quick course towards recovery, and which shows no signs of any notable disease in any organ, even in the liver itself.

This jaundice has been known and described from the earliest times, but it cannot be said that its nature and cause are even now beyond a doubt.

It is by far the most common of all the varieties of jaundice; it is probable that it is oftener seen than all the other varieties added together.

A surfeit of food, especially if indigestible, and, above all, a fit of drunkenness, are apt to be followed by a gastric catarrh and a jaundice. In these cases the ætiology of the jaundice would be said by many to be clear. In some the vomiting may come on after exposure to bad smells,* or other unwholesome influences, as is well seen in cases of simple jaundice, which, when numerous enough, are called epidemic jaundice, but are not uncommonly seen in single cases. Then there is a jaundice which follows mental emotions of all sorts, the old *icterus ex motu animi*. This cause of jaundice is said to be so firmly held by the vulgar in Germany that all cases are unhesitatingly set down to mental emotion.[*] In the older writers there will be found many cases of jaundice immediately following great mental emotion;[†] there are cases of prisoners becoming yellow at the moment that sentence of death was pronounced upon them; of two young men about to fight a duel, when one of them saw the other become so yellow, that being astonished, he ceased to fight; of a young priest, frightened by a dog, falling half dead, and being taken up yellow as saffron: of a young soldier, who, being struck in a public place, attempted to return the blow, but, being hindered by the bystanders, became jaundiced almost at that instant, and soon after fell into a fever and delirium, and died in the midst of convulsions.[‡] All these cases seem to me capable of quite a different interpretation; the pallor caused by excessive fear is often yellowish; and may have been easily mistaken by inexperienced or careless observers for a true jaundice.[§] In none of the cases does a careful examination seem to have been made; nothing is said about the conjunctiva or the state of the urine. It is, however, otherwise with the cases in which an interval, of days or weeks perhaps, comes between the emotion and the appearance of the jaundice. To these credence may be given, though whether the emotion be a cause of the jaundice remains to be discussed. Some of these cases are quite classical, and are quoted everywhere.[*]

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* Powell (*Observations on the Bile and its Diseases*, Lond. 1800. p. 77) says that medical students are often seized with the jaundice soon after they begin to work in the dissecting room. Powell seems to attribute this to the posture and confinement necessary for this study. I have not myself observed medical students to be more often jaundiced than others; but if it were a fact, I should attribute it rather to the bad sanitary state, as I have often seen persons exposed to bad smells and the like, jaundiced.

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[*] Frerichs, *Klinik d. Leberkrankheiten*, Braunschweig, 1858. Bd. i. p. 166 note. The same notion prevailed in England; as Shakspere can testify:

> "Creep into the jaundice
> by being peevish."
> *Merchant of Venice*, I. i.

> "What grief hath set the jaundice on your cheeks?
> *Troilus and Cressida*, I. iii.

[†] I do not think that Horace meant to speak of jaundice when he describes the following effect of jealousy:

> Quum tu, Lydia, Telephi
> Cervicem roseam, cerea Teleph
> Laudas brachia, væ meum
> Fervens difficili bile tumet jecur.

(*Carm.* Lib. i. *Od.* xiii.) The poets contain many allusions to the liver, as it was the seat of the emotions, love, courage, &c.

[‡] Portal, *Observations sur la nature et le traitement des maladies du foie*, Paris, 1813. p. 141.

Villeneuve, *Dict. des Sciences méd.* Paris, 1818. t. xxiii. p. 419.

[§] The jaundice described by Sydenham (*Obs. Med.* iv. 7. Greenhill's ed. p. 202) as seen in hypochrondriac men and hysterical women, must, I venture to think, be put down to gall stones rather than a nervous affection. In this opinion Heberden shares: "No reasonable deference to this accurate observer can make anyone much doubt of his having been mistaken." (*Comm.* Lond. 1806. Third ed. p. 240.)

Sir Thomas Watson[†] and Dr. Bence Jones[‡] supported the theory that mental emotion was a cause of jaundice.

In certain cases no cause whatever can be discovered. The season of the year has some influence; simple jaundice is more common in the spring and fall, particularly the autumn.

In simple jaundice, the first notice that the patient is ill is often the sight of his own face in the glass, or the being told by others of his yellow colour. This may happen on rising in the morning, and the patient then finds that he has lost appetite and feels sick; or he may even vomit. In a certain number of cases, the gastric symptoms come on later, even three or four days after the jaundice. In other cases, the greater number, perhaps, the gastric symptoms appear before the jaundice, a day, a week, or even longer.

When the gastric symptoms are not marked, there are sometimes signs of an intestinal catarrh, diarrhœa, or tape worm, and the like.

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[*] Dr. Wilks has recorded a case of jaundice which he appears to think due to emotion, the patient having been much frightened five days before the jaundice came on. There were, however, at the same time, headache, nausea, and slight diarrhœa. (*Brit. Med. Journal*, 1870. Vol. ii. p. 4.) In the same volume (p. 547) Mr. Churton has published a case in which "acute hepatic pain" and mental disturbance came together. The jaundice was treated with bromide of potassium, and recovery seems to be attributed to the use of this remedy. Dr. A. W. Foot (*Dublin Journal of Med. Science*, 1874. Vol. lvii. p. 217) and Ferber (*Arch. d. Heilkunde*, 1868. p. 558) have also published cases which they set down to emotional causes.

[†] Sir Thomas Watson, *Lectures on the Principles and Practice of Physic*, Lond. 1857. 4th ed. vol. ii. p. 609.

[‡] Bence Jones, *S. George's Hosp. Reports*, 1866. vol. i. p. 193.

Frerichs found that out of 41 cases of simple jaundice symptoms of a gastro-intestinal catarrh were present as *prodroma* in 34.[*] In my own cases, the proportion is nothing so great; but my figures, I must own, prove little or nothing. They were taken from out-patients; and many of the cases I saw only twice or three times, so that I was unable to verify my diagnosis by seeing the recovery of the patient.

It must be owned that in certain cases, no other symptom save that of jaundice can be found out. The patient says that he is in good health, saving only his yellow appearance, and applies for medical help purely on account of his yellow colour.

With the gastric symptoms there commonly set in, especially with women, giddiness, headache, and a sense of weakness or feebleness, which may be so great that a febrile disorder may be thought of, typhoid or the like. There is not unfrequently a slight rise in the temperature, which rarely passes above 100°. The tongue is usually coated with a white fur; there may be diarrhœa or constipation, and the fæces are colourless. The pulse usually preserves its natural number of beats. In women it may even be a little quicker; in some cases it becomes slow, as 60 or 65; and in rare cases it may sink lower, even to 40. Itching is often seen; xanthopsy rarely.

On physical examination, the liver will as a rule be found slightly enlarged, and the right hypochondriac and epigastric regions somewhat tender to pressure. Gerhardt has pointed out the importance of being able to feel or percuss the enlarged gall bladder,[†] this, however, is not always possible; as the shape and position of the reservoir are not constant. When made out, it is an important sign of obstruction to the common duct.

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[*] Frerichs, *Klinik d. Leberkrankheiten*, Braunschweig, 1861. Bd. ii. p. 418.

[†] Gerhardt, *Ueber Icterus gastro-duodenalis*, in Volkmann's *Sammlung klinischer Vorträge*, Leipzig, 1870-75, p. 107.

Bamberger states that pulmonary catarrh is very often an accompaniment of this simple jaundice.*

A simple jaundice always ends in recovery, and the first sign of convalescence is said to be a return of the appetite. Bamberger notes during convalescence a *fames canina* like that seen after typhoid.

The disease may last as short a time as a week or ten days; or be prolonged to three and even four months. After two months, great suspicion must rest on the diagnosis. The average appears to be three to four weeks.

As the disease never ends in death, but always in recovery, there are no opportunities for examining the cause of the jaundice by the help of anatomy, unless the life of the patient be ended by accident or some other disease; in this last case the observation will not be quite free from suspicion. The cause of the jaundice therefore remains unknown, and it is only by a comparison with like diseases and states, that any light can be thrown on the matter.

One point only is tolerably certain; that the bile does not find its way into the duodenum, as shown by the colourless state of the stools; and in those cases in which the gall bladder is found distended, it may be asserted that the hindrance is in the common duct. All beyond this is little better than conjecture.

The conjecture which found greatest favour during the last century as an explanation of simple jaundice, was the view that there was a spasmodic contraction of the bile ducts. This contraction became so great that it was impossible for the bile to pass down the ducts, no cavity being left, but merely a solid ligament.

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* Bamberger, *Krankheiten des chylopoëtischen Systems*, in Virchow's *Handb. d. spec. Path. u. Ther.* Erlangen, 1864. 2te Aufl. p. 566.

After death, the spasm relaxed, and no traces of its existence could be found in the body. This idea of an *icterus spasmodicus* or *spasticus* would explain all those cases in which no palpable obstruction to the ducts was discovered, and could therefore be applied to those for which now-a-days the theory of a hæmatogenous jaundice, or the like, is brought in. The existence of a spasmodic jaundice was accepted by Peter Frank,* and many others ; Cullen says : "such spasm may happen either in the duct itself, which we suppose to be contractile, or in the duodenum pressing the sides of the duct close together.†" The theory was used by Brüning to explain the appearance of *icterus epidemius*, and has continued down into our own time in vogue as a possible explanation of some kinds of jaundice.‡ It may be found even now spoken of here and there by certain French authors.§ Sir Thomas Watson says we can neither prove nor disprove it.‖

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* Peter Frank, *de cur. hom. morb. epitome*, Viennæ, 1821, Lib. vi. Pars iii. p. 320.

† Cullen, *First Lines of the Practice of Physic*, § MDCCCXVIII. Thomson's edition, Vol. ii. p. 656.

‡ Brüning, *de ictero spasmodico epidemico infantum Essendiæ*, Vesal. et Lips. 1773, quoted by Joseph Frank, *Prax. med. univ. præc.* Lips. 1843, Pars iii. Vol. ii. Sect. ii. t. i. p. 311.

§ Gubler, *Gaz. méd. de Paris*, 1854, p. 218.

‖ Watson, *Lectures on the Principles and Practice of Physic*, Lond. 1857, 4th ed. Vol. ii. p. 609.

Howship has recorded a case in which he thinks he detected constriction of the ducts after death. A young man, aged 18, died after 48 hours of excruciating pain in the seat of the gall-bladder. After death the liver was found quite natural, the gall-bladder large, tense, and full. The large and small intestines contained a white mucous matter, but no trace of bile. The *ductus communis* being punctured with a lancet about its middle, a very small probe, with some difficulty, passed through it into the bowels. In the opposite direction it passed with tolerable ease by the hepatic duct into the liver. Howship found, dissecting still further, the impervious duct solid, contracted, tough, and opaque, like a soft ligamentous structure. After six hours and later the ducts had become perfectly relaxed. (*Practical Remarks on the Discrimination and Appearances of Surgical Disease*, London, 1840. p. 194.)

There is no mention of delirium ; the skin was mottled as in scarlatina with an appearance of petechiæ ; spots of blood in the stomach under the villous lining. It was not apparently a case of *icterus gravis*.

The hypothesis of *icterus spasmodicus* depends on the possible irritability of the bile ducts, and the hypothesis has therefore risen or fallen in favour according to the views taken of the presence of muscular fibres in the ducts leading from the liver.

It still seems to be an open question whether the ducts can be excited to contraction and whether they contain involuntary muscular fibres.

Magendie gave a great blow to the theory when he stated that he had never been able to see a trace of contraction in the gall ducts of mammals after any excitant.[*] It is denied by many[†] that the ducts contain any contractile elements; and those who do admit that muscular fibres are present, state that the developement is very small and that it is not likely that they would be able to affect the bore of the duct.[‡] Others maintain that the ducts are irritable, and contract on the application of various stimuli.[§]

Heidenhain was induced, from the irregularity with which the bile made its appearance in some of his biliary fistulæ, to enquire if the ducts really possessed contractile fibres. He thinks he has proved their existence. He placed the ducts, fresh from the animals, in a large volume of absolute alcohol for 24 hours; sections were laid for a few hours in chloride of palladium. (1:900) In a few hours, the sections were mounted in water or glycerine. The cylindrical epithelium could be seen well preserved. Under it was a well-marked layer of a yellow colour, the elements of which ran, for the most part, in a circular direction, and in which numerous long nuclei were visible. Abundance also of longitudinal elements could be seen, not, however, clearly separated from the circular. The elements in the bundles of these circular fibres, might readily be taken for lymphoid cells, as there was often seen plainly a dark nucleus surrounded by brighter cell substance. With this marked layer was also a certain amount of connective tissue.

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[*] Magendie, *Précis élémentaire de Physiologie*, Paris, 1836, 4e éd. t. ii. p. 475.

[†] Henle, *Handb. d. system. Anat. des Menschen*, Braunschweig, 1866, Bd. ii. p. 217. Frey, *Handb. d. Histologie u. Histochemie*, Leipzig, 1867, p. 553. Cruveilhier, *Traité d'anatomie descriptive*, Paris, 1865-68, t. ii. p. 201.

[‡] Kölliker, *Handb. d. Gewebelehre des Menschen*, Leipzig, 1867, 5te Auflage, p. 440. Leydig, *Lehrb. d. Histologie*, Frankfurt a. M. 1857. p. 356.

[§] Longet, *Traité de Physiologie*, Paris, 1869, 3e éd. t. ii. p. 308. Colin, *Traité de Physiologie comp.* Paris, 1871, 2e éd. t. i. p. 785. Colin admits that the contraction is so feeble that no change in the diameter of the tube would be brought about. Henle (*loc. cit.*) was unsuccessful in his attempt to cause contraction of the ducts in a man recently beheaded.

If it be true, as F. E. Schulze teaches, that only the contractile fibres are coloured yellow by palladium, then it follows that the thick well-marked layer, described by Heidenhain, is made up of these fibres.

Heidenhain also noted, in an experiment on a rabbit, that the flow of bile was much increased when the aorta was compressed. Now this may mean that the ducts of the liver contracted, as contractions of the bowels and uterus are also noted whenever the aorta is compressed.*

Audigé has reviewed the evidence of the contractility of the ducts, and like Heidenhain, has come to the conclusion: i. that there are muscular fibres in the bile ducts both of men and dogs; and ii. that the ducts of dogs show a notable contraction under the stimulus of electricity, or mechanical means. Audigé, nevertheless, will not admit of a spasmodic jaundice; but applies his view of spasm of the ducts to the cases in which a gall stone is coming down from the bladder.† Dujardin-Beaumetz has indorsed Audigé's observations.‡

It will be seen, therefore, that even those who assert the existence of muscular fibres in the ducts, and their contractile power, do not allow of the theory of *icterus spasmodicus*. Still, nervous influences upon the liver must not be lost sight of, so long as injury to the fourth ventricle of the brain, or to the sympathetic in the neck may work such results. It is true that it is the only instance known; but the influence of the nervous system upon the functions of the liver would probably form a rich field of research for the physiologist.[*] Vulpian believes that jaundice from emotion may be caused by a catarrh of the ducts, by an abundant polycholia, or by an inversion of the movement of the bile generated in the liver cells. He thinks it likely that the jaundice is catarrhal in the greater number.[†]

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* Heidenhain, *Studien des phys. Inst. zu Breslau*, Leipzig, 1868. Heft iv. pp. 242-246.

† Audigé, *Recherches expérimentales sur le spasme des voies biliaires*, Paris, 1874.

‡ Dujardin-Beaumetz, *Bulletin de Thérapeutique*, 1873. t. lxxxv. p. 385.

By the side of the spasmodic jaundice may be considered the paralytic jaundice, which was once thought to be due to a stagnation of the bile in the ducts, brought about by the gall ducts and gall bladder not having contracted to expel their contents.[‡] This theory of jaundice was used by Th. von Dusch as an explanation of acute yellow atrophy, the cells of the liver being dissolved in the accumulated bile.[§] Both these theories are now discredited.

Another explanation of the cause of simple jaundice, held in much favour at the present day, is that it is due to an extension of the catarrh of the duodenum and stomach to the common duct. The presence of symptoms of gastric disturbance undoubtedly lends much colour to this theory; and in my opinion it is in no way discredited by the criticisms of Sée, which are to the effect that the stomach symptoms are not always those of gastric catarrh.[*] This is quite true; and there are some cases of simple jaundice in which there are no gastric symptoms whatever.

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[*] Heidenhain (or his pupils, *Arch. f. Anat. und Phys.* 1860. p. 667) is inclined to admit of an *icterus spasticus*, chiefly because the pressure under which the bile passes down the ducts is so small, and thus even a slight constriction would be enough to cause jaundice.

[†] Vulpian, *Cours sur la Bile*, 1874. Paris, recueilli par Paulier, p. 139.

[‡] Erasmus Darwin, *Zoonomia*, Vol. ii. § xxx. Lond. 1801. Third ed. p. 3.

[§] Th. v. Dusch, *Untersuchungen u. Experimente als Beitrag zur Pathogenes des Icterus*, Leipzig, 1854. p. 37.

It is commonly said by the Germans that Stokes of Dublin was the first to teach the theory of *icterus catarrhalis;* but it certainly seems that van Swieten had some notion of the doctrine. He attributes the jaundice of the new-born to the thick meconium adhering to the walls of the duodenum; and says that even in grown-up people a mucous secretion remaining in the upper part of the intestine has been the cause of jaundice; and he gives the old quotation from Hippocrates to show that jaundice arising from phlegm is little dangerous and easily cured.[†]

It is sometimes said that Dr. John Hunter (not to be confounded with the great John Hunter, the Surgeon,) spoke of jaundice from catarrh or mucus in the ducts. He is speaking of the cause of the jaundice in remittent fever and says: "In the body of a person who died of pulmonary consumption, I had lately occasion to observe some things not altogether foreign to the present subject. A few days before death, to the common symptoms of the disease, was superadded a jaundice. The lungs were found diseased in the usual manner; there were adhesions to the pleura, tubercles, indurations, and suppurations in their substance. In the abdomen there were marks of superficial inflammation all over the liver, and the lower surface of it was united to the stomach by adhesions. The gall-bladder was full, but no bile could be squeezed out of it. On laying the *ductus communis* open from the *duodenum*, it was found filled with bile of a brown colour, and of a thick and ropy consistence, as were also the *ductus hepatici*. Part of the *ductus cysticus* was laid open, and the gall-bladder was pressed with considerable force, but still no bile flowed. Through a blow-pipe introduced into the duct, the air at last with some difficulty was forced into the gall-bladder, after which by pressing again, a coagulum of bile was squeezed out, and what followed was ropy and black, like melasses. On laying the duct open all the way to the bladder, there appeared no other obstruction to the bile than the coagulum, which, as well as the thick and ropy state of that secretion, appear rather to have been the effects of stagnation than a cause of obstruction in the first instance. Did the inflammation in the neighbourhood of the ducts, and perhaps extending to them, excite such contractions in them as obstructed the bile, in the same way that a suppression of urine, is sometimes a consequence of inflammation, in the urinary passages?"[*]

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[*] Sée, *Gaz. d. Hôp.* 1872. p. 201.

[†] G. van Swieten, *Comment.* § 950. Lugd. Bat. 1755. t. iii. p. 128. "Imo et in adultis pituitosa colluvies in primis viis hærens, icteri causa fuit."

Portal also says that a swelling of the duodenal glands from inflammation or any other cause, may bring about a jaundice by hindering the flow of bile into the duodenum.[†]

When Broussais taught that all diseases were more or less due to gastritis or duodenitis, it was necessary that diseases of the liver and ducts should follow the rest. Andral is one of the writers who have carried out this view. Several times, he says, he has found in the bodies of jaundiced persons no other change than a violent inflammation of the duodenum, which appeared to have extended to the bile ducts.[‡]

It was maintained by Stokes in his Lectures on Medicine, that the most important and most frequent cause of jaundice was disease of the mucous surface of the stomach and duodenum. It is not, however, due to any mechanical hindrance to the flow of bile, but to a "sympathetic irritation" of the liver, secondary to the gastritis. The biliary secretion is arrested. Stokes' theory is thus nothing more than the theory of jaundice by suppression, but the suppression is due to "sympathetic irritation" of the liver from the stomach.* Budd, on the other hand, really noticed a catarrhal plugging of the ducts: "It happens, however, not very unfrequently, that, on squeezing the hepatic ducts, a viscid whitish fluid oozes out, which, on examination through the microscope, is seen to be chiefly made up of the prismatic epithelial cells of the gall ducts."† Further: "many of the cases of simple jaundice coming on in healthy persons are probably cases of this kind." But later on he says: "In a large proportion, perhaps in the greater number of cases, jaundice results primarily and solely, from the secretion of bile being suppressed or deficient."‡ This explanation of simple jaundice as a jaundice by suppression was in great vogue twenty years ago, and even now traces of the doctrine may be met with, rather, however, in speech than in print.

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[*] John Hunter, M.D. *Observations on the Diseases of the Army in Jamaica*, London, 1796, See Ed. p. 158.

[†] Portal, *Observations sur la nature et le traitement des maladies du foie*, Paris, 1813, p. 154.

[‡] Andral, *Clinique méd.* Paris, 1839, 4e éd. t. ii. p. 290.

But the writer who has done the most to advance catarrh of the bile ducts as a cause of simple jaundice to the favour in which it is now held by so many, is Virchow. This is another instance of a man, later on in life, destroying the work of his earlier days; for if the theory of hæmatogenous jaundice were received by any one, it was owing to the support which Virchow gave to it thirty years ago, on his entrance into life.§ But in 1865, Virchow declared himself in favour of the doctrine that jaundice arises always from the absorption of bile secreted beforehand, and showed from his experience that in many cases, unsuspected before, a catarrh of the ducts, or at least some obstruction to them, might be seen after death, if it were only carefully looked for.* This was at once taken up and applied afresh to the explanation of simple jaundice, and it certainly seems to me the best of all the theories which have yet been proposed. That a catarrh is a common cause of jaundice cannot I think be disputed, but that it is the cause of all cases of simple jaundice still lacks proof; a difficulty not likely to be overcome soon, as opportunity for examination after death is so rare.

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* Stokes, *Lond. Med. and Surg. Journal*, 1834. vol. v. p. 198.

† Budd, *On Diseases of the Liver*, London, 1845. First edition, p. 150.

‡ Budd, *op. cit.* p. 383.

§ Virchow, *Gesamm. Abhandl.* Hamm, 1862, 2te Aufl. p. 849.

Another explanation of simple jaundice has been set forth by Glax. The jaundice arises from changes in the circulation of the liver. These changes are due to the atony of the walls of the stomach and intestines, which so often show disorder in simple jaundice. If the tone of the walls of the stomach and intestine be decreased, the rapidity of the blood stream in the portal vein is decreased. This being the case, should any increase in the arterial pulsations appear, the ramifications of the hepatic artery, the portal vein, and the ducts in the liver will be pressed together; something must give way, and so the ducts which offer the least resistance suffer; the bile therefore passes into the central vein of the hepatic lobule.†

This theory would become more interesting if there were any evidence of the decrease of the rapidity of the stream in the portal vein. It would seem, however, probable, that if there be a catarrh of the stomach and intestines, there would be a greater flow of blood to them; and that the current in the portal vein would not be thereby decreased in rapidity. If, however, it can be shown that there is a decrease in the pressure of the blood in the vessels of the liver, I do not see any objection to the adoption of Frerichs' theory,* of which, however, Glax does not seem willing to avail himself.

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* Virchow, *Arch. f. path. Anat.* 1865, Bd. xxxii. p. 117.

† Glax, Virchow and Hirsch's *Jahresb. f.* 1875, Bd. ii. p. 235. Abstract from *Sitz.-Ber. des Vereins der Aerzte in Steiermark*, 1873-74.

Diagnosis. This is often a matter of some difficulty, and may be only cleared up by the recovery of the patient, when it becomes plain that the jaundice was simple.

Disease of other organs should be carefully excluded, especially of the heart and lungs. I have known the jaundice of nutmeg liver mistaken for a simple jaundice. Then the liver itself must be carefully examined, and if possible the state of the gall-bladder made out. Should this be found distended, and the liver not greatly enlarged, a certain advance is made in the diagnosis, and then if the patient be young and formerly in good health, and the gastric symptoms and freedom from pain well marked, the diagnosis may, with some likelihood, be made of simple jaundice.

The absence of pain is the great distinguishing feature in a diagnosis between simple jaundice and gall-stones. The liver in gall-stones is also much greater in size, the jaundice sets in after an attack of pain, and the staining of the skin and urine is much deeper. Simple jaundice shows little besides the staining of the tissues and the gastric symptoms.

Prognosis. If the diagnosis can be safely made, the prognosis becomes exceedingly good. But even in the mildest case, the mind of the practitioner cannot be quite easy; for it is these apparently typical cases of simple jaundice that now and then develope all the symptoms of *icterus gravis.*[*] Until the grave symptoms come on there is no means whatever of distinguishing between ordinary simple jaundice and the jaundice which is the forerunner of *icterus gravis.* The line which separates these two must be very narrow. The same poison, such as a foul smell, which gives to one person a gastric or intestinal catarrh with jaundice, seems to lead in another to the same disorder, but with the addition of parenchymatous degenerations in all the glands and muscles, as well as of the stomach. It seems to be a question of degree, not of kind.

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* Frerichs, *op. cit.* Bd. i. p. 89.

Treatment. It would be unwise to treat actively a disease which naturally ends in recovery. The treatment must therefore be limited to that which will certainly do no harm, and it will be profitable to keep the gastric symptoms only in view and to treat them. It is most important to avoid all means that may aggravate the state of the patient. For instance, a mercurial purge may be given at the onset of the disorder, if such be indicated by the sluggishness of the patient's bowels. But the repetition of this dose, or the daily administration of mercury, such as now and then may be heard of, is a serious damage to the patient. The same may be said of antimony, chloral, or any other drug which causes a parenchymatous degeneration of organs. For it will be impossible to tell how far from, or how near to, the border line that separates *icterus gravis* from simple jaundice the patient is, and the introduction of such a body as mercury into the œconomy may determine the arrival of the graver symptoms.

The best plan of treatment would seem to be to begin with a purgative, if the patient's bowels should not be already too much open. The purgatives may be vegetable; the compound colocynth pill of the pharmacopœia; or to which a few grains of calomel may be added. Alkalies may then be administered, with bismuth, before food. The diet should be strictly regulated. All indigestible matters, as vegetables and fruit, must be forbidden; and the diet restricted to milk, soups, without vegetables, or in which vegetables have been boiled, and then strained out, and some small amount of farinaceous food. Coffee, tea, and alcohol must be forbidden. The patient may be allowed acid drinks, such as lemonade. As the gastric symptoms subside, white fish and then meat may be allowed, and the alkaline treatment may be changed to a course of *aqua regia*.

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[*] Icteri nunquam spernendi, nam sub larva ac persona icteri saepe magni, periculosi, ac repentini morbi absconduntur; et saepissime moriuntur derepente icterici, ut ait Dodonaeus. (Stoll, *Aphorism.* in *Rat. Med.* Viennæ, 1790, Pars vi. Sect. i. § 103. p. 29.)

Emetics have long been a favourite remedy, and Sir Dominic Corrigan specially praises ipecacuan, by the action of which he thinks he has warded off the onset of the graver symptoms, and even cured a case of acute yellow atrophy.* I must own that ipecacuan, still more tartar emetic, appear to me dangerous remedies; for the diagnosis must be indeed certain before emetics can be given with confidence. They are supposed to act by compression of the gall-bladder and forcible expulsion of its contents into the duodenum. The serious results of violent efforts at vomiting, if a wrong diagnosis should chance to have been made, need scarcely be pointed out; if the ducts be obstructed by a gall-stone, or the head of the pancreas enlarged, vomiting seems more likely to be followed by a rupture of the bile passages behind the stone than by any good to the patient. Again, as Bamberger has quite correctly pointed out,† jaundice is not an unknown sequence of the administration of emetics themselves.

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* Corrigan, *Dublin Hosp. Gaz.* 1845, pp. 69 and 71.

† Bamberger, *op. cit.* p. 568.

The same cautions must be applied to another method of treatment which Gerhardt has of late introduced, pressure and faradization of the gall-bladder. The employment of electricity is indeed not new, as Erasmus Darwin says that he gave half-a-score of smart electric shocks along the course of the bile ducts from a coated bottle to a man who had been jaundiced for six weeks, and the same day the stools became yellow.*

Gerhardt grasps the enlarged gall-bladder with his fingers, and endeavours to squeeze its contents out. He says that the gall-bladder may be felt gradually emptying itself, and a sort of fremitus appears to accompany it. After this, the gall-bladder can no longer be made out by percussion, and on the second day the fæces become coloured. Gerhardt also places one electrode over the gall-bladder, the other on the spine at a level with the first, and then passes strong induction currents between the two; after three or four days the stools become coloured.†

For my own part I should scarcely like to adopt such active measures. It would be altogether different if the advantage to the patient were to be great, as the taxis in hernia; but the disease here is a very mild one, and the remedy may possibly prove worse than the disease. I do not think that it is justifiable to expose the patient to the risk of rupturing the ducts or the gall-bladder; and if the theory of jaundice from catarrh of the stomach and duodenum be allowed, the primary disease would not be overcome by the ejection of the plug of mucus into the duodenum, but it is probable that the plug would be renewed, the catarrh remaining, as soon as the excess of bile had passed through the papilla. Indeed, the passage of the bile over the mucous membrane is not likely to aid its recovery.

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* Erasmus Darwin, *Zoonomia*, § xxx. Lond. 1801. 3rd Ed. Vol. ii. p. 2.

† Gerhardt, *Ueber Icterus gastro-duodenalis, in* Volkmann's *Sammlung klin. Vorträge* (*Innere Medicin,*) Leipzig, 1870-75, p. 112.

Krull recommends the daily injection of cold water into the rectum. He says it has been so successful that he has never had to repeat it more than seven times. One or two litres (from two to four pints) of a temperature of 60° F. (15° C.) are thrown up the bowel, and allowed to be retained as long as possible. The temperature of the water must be gradually raised with each successive injection.*

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* Krull, *Berlin. klin. Woch.* 1877, p. 159.

CHAPTER XVIII.

ICTERUS EPIDEMIUS.

Syn. *Vernalis*. Hippocrates speaks of a kind of jaundice which he calls epidemic, because it attacks at all seasons;[*] but it is only until a little more than a hundred years ago that epidemics of jaundice have been described.[†] Peter Frank says that such were noticed at Ghent in 1742, and at Mainz in 1754.[‡] Monro also speaks of an epidemic amongst the English troops quartered in North Germany in the winter of 1761-62.[§] In 1807, the year after the battle of Jena, and of much misery throughout Germany, several epidemics of jaundice have been spoken of; and after the siege of Paris, an epidemic was observed in 1871, both amongst the soldiers and the civil people.[‖]

The jaundice which becomes epidemic seems to preserve one type wherever it is found. It is that which may very properly be called simple jaundice. After some few days of gastric disturbance, want of appetite, nausea, or even vomiting, coupled with obstinate constipation or diarrhœa, jaundice sets in, the skin becoming yellow, the urine high-coloured, and the stools white. In some epidemics, however, the contrary has been prevalent, and the stools have been bilious. There appears in the greater number to be no enlargement of the liver.[*] As in simple jaundice, not epidemic, the greater part recover after an illness from one to five or six weeks in length.

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[*] Hippocrates, *De morb. int.* Cap. xxxvii. Littré's Ed. t. vii. p. 258. Ἄλλος ἴκτερος· ἐπιδήμιος οὗτος καλέεται, διότι ἅπαν ὥρην ἐπιλαμβάνει.

[†] There are several references in other writers to authors before this time. They are given at the end of this work. Some I have not been able to verify; and others seem to me in no way related to epidemic jaundice.

[‡] Peter Frank, *De curandis hominum morbis epitome*, Viennæ, 1821, Lib. vi. Pars iii. p. 298. Frank does not say he saw the epidemics, as Stokes asserts, (*Lond. Med. and Surg. Journal*, 1834, Vol. v. p. 199.) but speaks of them only from hearsay.

[§] Donald Monro, *An account of the diseases &c. in the Military Hospitals in Germany*, Lond. 1764, p. 208.

[‖] Portal seems to have noted something of this sort: "Combien les jaunisses ne sont pas fréquentes dans les villes assiégées? et combien n'en a-t-on pas vues dans les malheureux temps de la révolution?" (*Obs. sur la nat. et le traitement des maladies du foie*, Paris, 1813, p. 141.)

Jaundice has been seen as an epidemic in parts of the world widely separated from each other. Reports have come in from Smyrna, Martinique, Tennessee, Italy, France, Germany, England, preserving in all these countries and places its character of simple jaundice. It seized upon the well-to-do inhabitants of a town in the midst of a plain, like Greifswald, as well as the miserably poor artizans of a village surrounded by hills, like Lüdenscheid. Epidemics amongst soldiers are much spoken of; but in two of these, the jaundice was seen among the civil population as well: persons living in camps or barracks, mad-houses, prisons, and convents, that is, a large number living together, and under the same hygienic conditions, seem specially the subjects of the reports which come in. The largest number attacked in one epidemic was seen in the Bavarian army in cantonments to the south-west of Paris. From February to May, 1871. 799 soldiers fell ill of a simple jaundice, no less than 2·4 *per cent.* of the whole army. Similar epidemics were seen in the German army about Dijon, Poligny, and other places.[†]

In some cases, it has seized only upon grown-up persons, no one under 20 being attacked, or one or two children only being ill. In other cases, the children have been those chiefly to suffer.[‡] In other epidemics it is the pregnant women who suffer; and whenever this epidemic jaundice attacks pregnant women, it seems to go hard with them, causing either serious symptoms, as delirium and coma, or death itself, although the non-pregnant women and the men recover without trouble.[*] Premature labour usually comes on, and the child is born dead, but not yellow. In an epidemic in a house at Mainz, recorded by Stitzer, the women and not the men were those attacked.[†] In one epidemic among soldiers, only the recruits suffered.[‡]

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[*] Martin (*Recueil de mém. de méd. militaire*, 1860. iii. série, t. iii. p. 374) found that 43 out of 71 patients had enlarged liver, and 29 enlarged spleen. Dr. Hayden (*Med. Press and Cir.* 1869. Vol. viii. p. 4) found enlargement of the liver in the greater number.

[†] Seggel and Hiller, quoted by Robert Gollmer, *Ueber die Aetiologie des Icterus epidemicus*, Inaug. Diss. Berlin, 1877. pp. 9 and 10.

[‡] Rehn, *Jahrb. f. Kinderheilk.* 1870. Bd. iii. p. 197.

The epidemics have chiefly been at their height in cold weather, and during cold winds, though rarely they have been seen in summer, and in very hot weather;[§] to this hot weather they have been attributed, as was the epidemic in the French camp at Pavia.[‖] In some cases, the epidemic has been noticed when large ditches were emptied and cleaned as at Arras, or in towns and houses where the drainage has been bad, and bad smells prevailed, as at Greifswald and Rotherham. It was noticed in Paris after the siege. Other epidemics have been complicated by intermittent fevers and dysentery, and it is these which have proved most fatal, not merely to the pregnant women, but even to men. It should be remarked, however, that these cases of jaundice complicated by intermittent fevers, belong rather to febrile than to epidemic jaundice. The type of the epidemic is a simple jaundice uncomplicated by other disorders.

In other cases it has been thought due to the food or drink; especially if the soldiers have been long kept upon the same diet, of fresh or of salted meats.

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[*] Saint-Vel, *Gaz. des Hôp.* 1862. p. 538.

[†] Stitzer, Virchow and Hirsch's *Jahresb. f.* 1876. Bd. ii. p. 213.

[‡] Lindemann, *Centralblatt f. d. med. Wiss.* 1875. p. 96.

[§] Sir Thomas Watson speaks of a sort of epidemic of a mild and manageable kind of jaundice, which affected young persons, chiefly girls, between ten and sixteen years old, in London, in the autumn of 1846. just after the prevalence of extremely hot weather. (*Lectures on the Principles and Practice of Physic*, London, 1857. 4th ed. Vol. ii. p. 610.)

[‖] Martin, *Recueil de mém. de méd. mil.* 1860. iiie Série, t. iii. p. 374.

Carville has described, under the name of *ictère grave épidémique*, a number of cases of jaundice which he observed in a prison in the summer of 1859. Out of 47 persons attacked, 11 died. There was delirium in one case only; in the rest there seems a remarkable absence of nervous symptoms, if the cases are to be taken as *icterus gravis*. In many of them, a hæmorrhagic diathesis was present. In the fatal cases, the state of the liver is in all said to be natural. The microscope was not used to verify the state of the cells.*

It will doubtless be the opinion of many that it is impossible to allow the name of *icterus gravis* to this epidemic. The absence of nervous symptoms and of naked eye disease of the liver, which, although the microscope was not used, would have been plain enough if present, might seem to forbid it being classed among this variety of jaundice. The description given by the author is not at all clear: apparently belonging to the school of Louis, he has thought more of numbering his patients than of describing their symptoms. Trousseau says that the simple statement of the results appears to be in contradiction with the notions of general pathology.†

Very different is the epidemic described by Arnould and Coyne amongst the soldiers forming the garrison at Lille, in June 1877. About eight or nine became jaundiced, and the first four died, the first two within 12 hours of admission. The cases, which came into hospital at the end of the epidemic, although they suffered from severe symptoms, yet recovered. Nervous symptoms and hæmorrhages were present in nearly all. The only point wanting to complete the *post-*

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* Carville, *Arch. gén. de méd.* 1864. Vol. ii. p. 129.

† Trousseau, *Clinique méd.* Paris, 1865. 2e éd. t. iii. p. 279.

mortem account is the use of the microscope; a considerable omission, although the naked-eye appearances of the liver, and of the other organs, leave but little doubt as to the nature of the disease.*

Owing to the mildness of ordinary epidemic jaundice, no opportunity for examination after death commonly exists, and in those in which it has been made, no fresh light has been thrown on the subject. The majority of writers look upon the jaundice as due to a catarrh of the bile ducts, extending from the duodenum. Others attribute it to infection, to the action of miasma upon the body, begetting a mild form of acute yellow atrophy. Both of these explanations may be allowed, and applied to those cases to which they seem severally suitable.

The view of epidemic jaundice which commends itself most to my mind is that the disorder is the result of a poison introduced from without through the food, drink, or air. The dose of this poison may in some cases be small, or the poison itself may not be very active, exciting only a certain amount of gastric catarrh, one of the most common effects of poisons, and which extends into the duodenum and causes a jaundice. If the same food, drink, and air, containing the poison, be common to a large number of persons, as in camps and prisons, then an epidemic of jaundice takes place. But if the dose of the poison, whatever it be, be large, then the results seen in so many other kinds of poisonings take place. The glands and muscles of the body all degenerate, and the symptoms of *icterus gravis* are set up. This happens the more readily, if the degeneration have already made way in the tissues, as may be seen in the cases of pregnant women, whose tissues are already in a state of parenchymatous degeneration, and on whom therefore the poison causing the epidemic seems to act with increased severity.

The nature of the poison is obscure. In some cases it seems to be connected with the cleaning of trenches, bad drainage, and the like unwholesome doings.

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* Arnould and Paul Coyne, *Gaz. méd. de Paris*, 1878. p. 114.

Fritsch has described a very curious and interesting epidemic of purpura and jaundice combined, which prevailed at Civita-Vecchia in January, 1859. As to the cause of the epidemic, Fritsch is himself not clear, but thinks it a slight form of yellow fever. The jaundice was preceded by a short febrile attack lasting from two to four days. The purpura also usually appeared before the jaundice. Epistaxis and bleeding from the gums, as well as ecchymoses under the skin, were common. The spots of purpura appeared on the trunk and upper parts, rarely on the legs. Fritsch divides the disease into four stages: i. the febrile stage; symptoms of which were fever, headache, pains in the limbs, loss of appetite, &c., at the end of this stage the purpura appears; ii. the developement of the jaundice, lasting 2 to 6 days like the febrile stage; it was ushered in and accompanied by bleedings; and after every bleeding, the colour of the skin became darker; iii. stage of prostration; the bleedings and jaundice became less, but great weakness set in. This stage gradually passed into iv. the period of convalescence.

The urine contained abundance of bile pigment during the jaundice; the bowels were much bound. Quinine seemed of little value, and the treatment was directed chiefly to the symptoms.[*]

The treatment of *icterus epidemius* must vary according to the nature of the case. If a simple jaundice be diagnosticated, then the treatment spoken of under that jaundice should be used. If the symptoms of *icterus gravis* set in, they must be treated, although very little will then remain to be done.

The patients should be removed, if possible, into different surroundings.

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[*] Fritsch, Canstatt's *Jahresbericht f.* 1862. Bd. iii. p. 291. Abstract of a *Thèse de Strasbourg.*

CHAPTER XIX.

Icterus Gravis.

By *icterus gravis* I mean an acute jaundice, accompanied by nervous symptoms, delirium, coma, and convulsions, and by a hæmorrhagic diathesis. After death, there is found a cloudy swelling or parenchymatous degeneration of all the glands and muscles of the body, and probably also of the smaller arteries and capillaries. There is a great decrease or even entire absence of glycogen or sugar in the liver,[†] and it is also probable that the urea in the urine is very greatly diminished. Both these changes seem due to the injury inflicted on the cells, in the first place, of the liver, and in the second, of the body at large, while the hæmorrhages and the nervous symptoms are probably due to the degeneration of the vessels; the hæmorrhages, to those of the body at large; the nervous symptoms, to the degeneration of the cerebral vessels causing an imperfect supply of blood to the brain. The whole of these phænomena may, with some probability, be thought due to the action of a poison, either generated within, or brought from without, the body.

Admitting this definition of *icterus gravis* as a disease due solely to the parenchymatous degeneration of all the glands and muscles, it becomes evident that it is a disease, not of the liver only, but of the whole body; the liver often, indeed, shows the greatest amount of change, because it is the largest gland in the body; and the jaundice caused attention to be early paid to that organ. But *icterus gravis* is in reality a general disorder, as much as small-pox or typhoid is.

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[*] In simple fatty infiltration the amount of sugar is said to be increased.

There are not many varieties of *icterus gravis*: the two most important are the diseases called acute yellow atrophy of the liver, and phosphorus poisoning. Yellow fever is also a variety; and the "bilious typhoid" described by Griesinger, poisoning by antimony, arsenic, alcohol, and doubtless many other bodies, must follow under the same heading.

I must own that it seems to me of little profit, to discuss the question whether the anatomical changes seen in *icterus gravis* be inflammation or not. It will be seen that great pathologists, such as Bright and Virchow, have given the name of inflammation to these changes; but it seems to my mind that the word inflammation has so indefinite a meaning, that no information is given if a process be called by this name. If, however, the terms 'cloudy swelling' or 'parenchymatous degeneration' be used, then the nature of the appearance is at once understood: it is that the cells become swollen and filled with granules, some soluble and some insoluble in acetic acid; these granules being often present in such quantity as to obscure the nucleus. By the use of these names, the appearances perceived by the senses only are expressed and no inference is drawn from the facts. Later on, the cells become filled with granules insoluble in acetic acid, and soluble in æther, and therefore judged to be fat; or filled with large fat drops; or the cells may soon break up, and their walls no longer be distinguished, as in the liver in acute yellow atrophy.

There is, however, a host of other diseases in which a general parenchymatous change takes place: such are pneumonia, typhoid fever, puerperal fever, or any acute specific disease or any disease attended with fever. But in these disorders it is not common for the degeneration to go so far as in *icterus gravis*. The first stage of the process only is reached; and often only the liver and kidneys, and not the heart and muscles are attacked; or the liver only may show the change. Liebermeister, on the other hand, has shown that the last stage of the disease may be reached in disorders in which it was formerly quite unsuspected. He has found the liver cells dissolved, as completely as in acute yellow atrophy, in cases of puerperal fever, typhoid fever, pyæmia, and tuberculosis.[*] Acute yellow atrophy is therefore but the last expression of a process, the first beginnings of which may be so commonly seen in cases of pneumonia, typhoid fever, or any other febrile disease.

An outcome of the process in the liver, to which but little attention has been hitherto directed, is an overgrowth of the connective tissue. It can no longer be denied, for very competent histologists, such as Robin, Waldeyer, Winiwarter, and Georg Wegner have asserted that, in cases of acute yellow atrophy and phosphorus poisoning, there is a distinct cirrhosis of the liver. This appearance of cirrhosis would appear to depend upon the length of time that the disease has lasted. In slow poisoning by alcohol, cirrhosis is one of the most common appearances; and subacute poisoning by alcohol is one of the forms of *icterus gravis*. Analogy therefore would lead us to believe that an overgrowth of the connective tissue of the liver may well follow parenchymatous degeneration, whatever be its cause. This view is supported by a comparison of the parenchymatous degenerations seen in the kidney, which so commonly end in a chronic process of overgrowth of the connective tissue, the kidney of scarlet fever ending in the small red contracted kidney.[†]

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[*] Liebermeister, *Beiträge zur path. Anat. u. Klinik d. Leberkrankheiten*, Tübingen, 1864. p. 209. Oppolzer (reported by Schnitzler, *Deutsche Klinik*, 1859. p. 286.) seems to have noted the complete destruction of the liver cells in typhus before Liebermeister.

[†] Dr. Thomas Barlow says: "I am acquainted with one case, at all events, of

It may be asked: Is a parenchymatous degeneration of all the glands and muscles of the body possible without the clinical symptoms of *icterus gravis*? Can such changes take place without causing jaundice, or nervous symptoms, or hæmorrhages? A slight amount of change may take place without any severe symptoms; but when the degenerations are so far advanced as to cause the death of a patient without other complication, it is very rare indeed to find no jaundice nor nervous symptoms.

Some rare cases, a few instances in number, have indeed been recorded of death without any marked symptoms, and yet far advanced parenchymatous degeneration has been found after death.* In some the jaundice has been only noticed after death; and in others, no nervous symptoms.

ACUTE YELLOW ATROPHY OF THE LIVER.

The synonyms used in this disease are numerous. *Icterus gravis*, an expression which would first seem to have been used for this disease by Charles Ozanam as the French *ictère grave*,† *icterus malignus*, *perniciosus*, *typhoides*,‡ *toxæmicus*, *choletoxicus*. The Germans have called it *acute gelbe Leberatrophie*, *diffuse Hepatitis*, *acute parenchymatöse Hepatitis*.§ It is also called cholæmia, acholia, with reference to the theories of the suppression of bile or of the symptoms being due to bile in the blood. *Schwerer Icterus* is of course a translation of *icterus gravis*, for which there seems to be no good English equivalent. *Ictère malin*, and *ictère hémorr-*

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well-marked fibrosis of the liver, which dated from scarlet fever." (*Trans. of the Pathological Soc. of London*, 1877. vol. xxviii. p. 355.)

* Bamberger, *Krankheiten des chylopoëtischen Systems*, Erlangen, 1864. p. 532. note.

† Charles Ozanam, *de la forme grave de l'ictère essentiel*, Thèse de Paris, 1849.

‡ Lebert, *Arch. f. path. Anat.* 1854. Bd. vii. p. 343.

§ August Foerster, *Handb. d. path. Anat.* Leipzig, 1863. Bd. ii. p. 179.

hagique essentiel are also French synonyms for the disease.

Dr. H. C. Wood proposes to give the disease the name of leucinosis from the presence of leucin in the blood.[*] I am glad to find that in this he has no follower.

History of Acute Yellow Atrophy. There appears to be no account of this disease in the Greek,[†] Latin, or Arabic authors. I have not been able to find an earlier example on record than a case of Ballonius, an author who died in 1616. A boy, of noble birth, became sullen and obstinate; then jaundice, slight fever, and white stools were noticed. This state lasted about fifteen days. Suddenly delirium with convulsions came on, and he died. After death, the liver was found diseased, and ὑπόχλωρον.[‡] There is also a case from Guarinonius, of a Cardinal Sforzia (*sic*), who died in convulsions after a fifty-four days jaundice. The liver was found yellow.[§]

Franciscus Rubeus speaks of a young man, aged 22, who was jaundiced and fatuous; and who died at the end of the fourth day.[||] Vercellonus also describes his brother's case; he was threatened by a creditor, fell into a jaundice, and died in a few days.[¶] It must be owned that these cases are highly doubtful; and that the only one which could be defended with much chance of success is the case of Ballonius. Morgagni is really the first author to describe the disease so that it can hardly be mistaken. He records a case of Valvalva's; in which a young priest, after suffering a perturbation of mind, fell ill of the jaundice, attended with vomiting and pain at the pit of the stomach. The stools were white, and on the third day there were delirium and convulsions. The next day he was comatose, and he died at the end of the fourth day. The belly being opened, the liver was found flaccid and pale, and in the stomach were red spots. Another case apparently of his own observation, is this: a promising young man was frightened by a bully holding some kind of firearm before his chest. Next day he was jaundiced, then became delirious, convulsions set in, and he died in twenty-four hours from the beginning of the delirium. After death nothing was found.*

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[*] H. C. Wood, *American Journal of the Med. Sci.* 1867. vol. liii. p. 418.

[†] Hippocrates speaks of an acute jaundice killing rapidly, but the rest of his description does not coincide with this disease. (*De morb.* lib. iii. § 11. Littré's ed. t. vii. p. 131.)

[‡] Quoted by Bonetus, *Sepulchretum*, Genevæ, 1700. Lib. iii. Sect. xviii. Obs. 6 from Ballonius, *Epid. et Ephem.* Lib. ii. p. 244. a reference I have been unable to verify.

[§] Guarinonius, *Consult.* 94 and 95 in Bonet. *ibid.* additament. Sect. xviii. obs. v.

[||] Francis. Rubeus, *Noct. Exerc.* Hamburg. 1660. Ex. xv. p. 195. De ictero lethali.

[¶] Jacobi Vercelloni, *de bile aucta et imminuta*, in Bianchi's *Historia Hepatica*, Genevæ, 1725. t. ii. p. 794.

Morgagni also relates a case of a little girl, 5 months old, who was seized with fever and diarrhœa, and then with convulsions. On the fifth day jaundice came on, and she died. After death, "rectum atra nigredine infectum;" nothing in the chest or head.† It seems probable that the two first cases of Morgagni are really cases of acute yellow atrophy; but the last is very doubtful.

Maximilian Stoll relates a case which may well be one of acute yellow atrophy. A young man, 26 years old, became very sad, and lost his appetite for about eight weeks. Then jaundice appeared with white stools, and, after lasting about three weeks, fever came on with taciturnity and delirium. Death took place within a few days, the right arm being swollen and very painful. After death the bile ducts were found free, and all the organs flabby.‡

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* Morgagni, *de sedibus etc.* Ep. xxxvii. §§ 2 and 4.

† Morgagni, *op. cit.* Ep. x. § 7.

‡ Stoll, *Rat. Med.* Pars iii. Vienna, 1780. p. 358. Cf. p. 390. Villeneuve (*Dictionaire des Sciences méd.* Paris, 1818. t. xxiii. p. 419) says that Boerhaave records a case of a merchant who, receiving the news of the loss of one of his

The next observations on this disease were made, one after another, in a few years, in Dublin. Cheyne in 1818 published a case of jaundice, delirium, vomiting of a dark fluid, and death in three days from admission, and on the twelfth of the illness. After death, no disease was found in the liver or ducts; the spleen was large, and the kidneys large and mottled.[*] Similar cases of jaundice, delirium, and rapid death, and nothing to account for the jaundice, were soon after recorded by O'Brien[†] and Marsh.[‡]

About the same time, Martinet recorded in a boy of fifteen, an attack of jaundice with delirium; after death the liver was found smaller than natural and almost pulpy, of the colour of rhubarb, mixed with red streaks.[§] Villeneuve also mentions the case of a young soldier who received a blow in a public place, and, being hindered by the bystanders from avenging himself, he wearied himself in vain efforts to get at his adversary. Almost at the same moment he became jaundiced; he was seized shortly after with fever and delirium, and died in the midst of convulsions.[‖]

Abercrombie in 1821 saw a case of rapidly fatal jaundice. A lady aged 50 became yellow in the beginning of June without any apparent cause. On the 16th she began to vomit; and on the 19th streaks of black were noticed in the vomit, and she died on the morning of the 21st. After death the liver was found reduced to

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ships, was seized with jaundice, and soon died. Richard Powell, says he met "with two cases within a short time of each other, where a jaundice of some continuance was succeeded by decided apoplexy and death; the patients were both females, and young." (*Observations on the Bile and its Diseases*, London, 1800, p. 83.)

[*] Cheyne, *Dublin Hospital Reports*, 1818. Vol. i. p. 273.

[†] O'Brien, *Trans. of the Association of the Fellows and Licentiates of the King's and Queen's College of Physicians in Ireland*, 1818. Vol. ii. p. 500.

[‡] Marsh, *Dublin Hosp. Rep.* 1822. Vol. iii. p. 276.

[§] Martinet, *Biblioth. méd.* 1819. t. lxvi. p. 350.

[‖] Villeneuve, *op. cit.* p. 420.

one-third of its natural size, of a very dark, almost black colour, and soft like a mass of clotted blood. The stomach and bowels held a black matter.*

In 1836, Richard Bright, one of the first English physicians to record cases of acute yellow atrophy, published three very instructive examples of this disease.† They are the more important because he was the first to pronounce the word "inflammation" in describing the state of the liver. His paper is headed: "Observations on Jaundice, more particularly on that form of the disease which accompanies the diffused inflammation of the substance of the liver." The three are well-marked cases of acute yellow atrophy, so far as the symptoms and appearances to the naked eye after death are concerned, and the large gall-ducts in all were pervious and unstained by bile.

About the same time, C. J. B. Aldis in London,‡ Griffin in Ireland,§ and Alison in Edinburgh,|| published cases of rapidly fatal jaundice, which may, in the absence of evidence to the contrary, be looked upon as probably due to acute yellow atrophy. Twining, at this date, speaking of the diseases of India, says: "In some cases, I have known robust patients die with symptoms of oppressed brain, within 36 hours after the sudden appearance of intense Jaundice; for the accession of which last-named disease, no cause could be assigned."¶

The cases recorded by Andral of softening of the liver** are by some thought to belong to acute yellow

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* Abercrombie, *Pathological and Practical Researches on Diseases of the Stomach, &c.* Edinb. 1828. p. 336. Case cxxiv.

† Bright, *Guy's Hospital Reports*, 1836. Vol. i. p. 621.

‡ C. J. B. Aldis, *Lond. Med. Gaz.* 1834. Vol. xiii. p. 833.

§ Griffin, *ibid.* p. 801.

|| Alison, *Edinb. Med. and Surg. Journal*, 1835. Vol. xliv. p. 287.

¶ Twining, *Clinical Illustrations of the more important diseases of Bengal*, Calcutta, 1832. p. 258.

** Andral, *Clinique méd.* Paris, 1839. t. ii. p. 363 *et seqq.*

atrophy. I cannot say that I am able to share this opinion. The cases seem to me to be rather those of pyrexial softening, or of fatty infiltration, of the liver, than of acute yellow atrophy.

A few cases were observed in Germany, by Heyfelder,[*] Sicherer,[†] and Schönlein,[‡] but the chief observations were made in Vienna; and to the medical school of this great town we owe nearly all our early ideas of the disease. The Vienna physicians, and especially Rokitansky, the morbid anatomist, were the first to give a name to the disease and find it a place in the nosology.

The year 1843 is of much importance in the history of acute yellow atrophy. In that year Horaczek published the first monograph of the disease, in which all the cases known, to the number of one and twenty, are brought together and compared.[§] Rokitansky had just brought out his book on morbid anatomy, in which the appearances seen in the liver were described under the name of acute yellow atrophy; "the proper gland substance melts, is destroyed in the bilious deliquescence (*Gallen-Colliquation*), and disappears."[‖] I think it doubtful from this passage, and here I offer an opinion at variance with that of many others, that Rokitansky was acquainted with the destruction or solution of the liver-cells, now known to be so common in this disease. It was, however, in the very same year (1843) that Thomas Williams first recorded in plain terms the solution or disappearance of the liver-cells. This was not discovered in a case of acute yellow atrophy, but in a case of permanent long-standing obstruction to the ducts,* and the first case of acute yellow atrophy in which the destruction of the liver-cells was plainly made out is one recorded by Budd, in which the examination with the microscope was made by Mr. Busk.† Budd devotes in addition a chapter to this disease, calling it softening of the liver with suppressed secretion of bile, and bringing together many cases published before.

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[*] Heyfelder, Schmidt's *Jahrbb.* 1838. Bd. xx. p. 313.

[†] Sicherer, *ibid.* 1842. Bd. xxxv. p. 335.

[‡] Schönlein, *Klinische Vorträge*, Berlin, 1842. p. 308.

[§] Horaczek, *Die gallige Dyscrasie, (Icterus) mit acuter gelber Atrophie der Leber*, Wien, 1843.

[‖] Rokitansky, *Handb. d. path. Anat.* Wien, 1842. Bd. iii. p. 313.

Although single cases had been recorded in Paris by several French physicians, as by Rayer in 1845,‡ and Baudon in 1847,§ yet Charles Ozanam's thesis may be looked upon as the foundation of the French observations upon acute yellow atrophy.‖ Ozanam was the first to apply the term *ictère grave* to this disease, a name which has become very common indeed in France, but without much discrimination. The thesis itself is, for the time at which it was written, wonderfully complete, and deserves far greater praise than the competing treatise of Horaczek's.

From this time onward single observations multiply in England, France, and Germany; detailed with more or less accuracy. In 1854-55, Lebert published an account of all that had been done before him, and at the end of which, in somewhat hesitating fashion, he announced his inclination to believe that acute yellow atrophy is a general disorder. Indeed the name of *typhus icterodes* or *icterus typhoides* sufficiently indicates this.¶ But a year before, Buhl had published his case and distinctly compared the process in acute yellow atrophy to typhus, yellow fever, pyæmia, and the like,** and Buhl was thus the first to look upon acute yellow atrophy as a general disorder. In the same year, Th. von Dusch set forth his theory of the solution of the liver-cells in their own secretion, as the cause of acute yellow atrophy;[*] a view promptly disowned by Robin, who, in turn, was the first to point out the increase of the connective tissue in the liver seen in some cases of acute yellow atrophy.[†] About the same time Foerster attempted a classification of cases based upon morbid anatomy, a division which does not indeed now hold good, but doubtless did service in its own day. He divided the cases into four kinds: i. those in which a poisoning of the blood is the primary disease, as in pyæmia, puerperal fever, and in the tropical miasmatic fevers; ii. those cases in which a permanent hindrance to the flow of bile from the gall-ducts into the duodenum exists; iii. those cases in which no hindrance to the flow of bile exists, but the same destruction of the liver-cells takes place; iv. those cases in which there is no jaundice of the liver, nor mechanical hindrance to the flow of bile, but the liver itself is wasted, with destruction of the liver-cells, an acute parenchymatous inflammation of the liver.[‡] Nowadays one would be inclined to abolish all Foerster's distinctions between the different classes, except of course the second, and to look upon all as really forming but one kind of disease. The second class cannot be admitted in any degree amongst those which should be called acute atrophy.

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* Thomas Williams, *Guy's Hospital Reports*, 1843. p. 444.

† Budd, *On Diseases of the Liver*, London, 1845. First ed. p. 205.

‡ Rayer, *Gaz. des Hôp.* 1845. p. 369.

§ Baudon, *Bulletin gén. de thérapeutique*, 1847. t. xxxiii. p. 299.

‖ Ozanam, *de la forme grave de l'ictère essentiel*, Thèse de Paris, 1849.

¶ Lebert, *Arch. f. path. Anat.* 1854. Bd. vii. p. 343 and 1855. Bd. viii. p. 147.

** Buhl, *Zeitschrift f. rat. Med.* 1854. N. F. Bd. iv. p. 355.

Monneret, who paid some attention to diseases of the liver, pointed out in 1859 the hæmorrhagic diathesis which accompanies acute yellow atrophy,[§] and in the same year Rokitansky published his cases of synchronous fatty degeneration of the liver and kidneys; cases from which he infers that kidney disease always accompanies acute yellow atrophy, and that the nervous symptoms are due to uræmia. These cases are also interesting from one of them being a case of phosphorus poisoning.* It is the first time that phosphorus poisoning appears in the history of acute yellow atrophy. Hereafter the two will be considered together, until at last the more venturesome assert their complete identity. A little before this time Frerichs brought out the first volume of his book on liver diseases; he calls acute yellow atrophy, *acholia*, or suppression of the functions of the liver,† and details many cases which he himself had watched. He directed attention to the state of the kidneys, an organ which he says has received less notice in this disease than it deserved, an idea which Rokitansky took up in the paper which has just been spoken of.

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[*] Th. v. Dusch, *Untersuchungen und Experimente als Beitrag zur Pathogenese des Icterus*, Leipzig, 1854.

[†] Robin, *Mémoires lus à la Soc. de Biologie*, 1857. p. 9.

[‡] Foerster, *Arch. f. path. Anat.* 1857. Bd. xii. p. 353.

[§] Monneret, *de l'ictère hémorrhagique essentiel*, Paris, 1859.

Wunderlich soon after attempted a classification from a clinical standpoint. He makes no less than six different kinds: i. cases in which, with the onset of the disease, appear symptoms like those of the onset of a fever or exanthema, and with the appearance of the jaundice these symptoms cease; ii. cases which begin with symptoms becoming more or less rapidly serious; jaundice appears in their course; death soon takes place and nothing is found in the body; iii. cases which begin with severe symptoms, rapidly increase in severity, and soon die; after death a molecular destruction of the liver tissue is found; iv. cases which begin with all the violence of poison, slight jaundice, rapid death, after which no decrease in size of the liver, but an increase, and great deposit of fat in its cells: v.

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* Rokitansky, *Zeitschrift d. k.k. Gesellschaft d. Aerzte zu Wien*, 1859. p. 497.

† Frerichs, *Klinik d. Leberkrankheiten*, Braunschweig, 1858. Bd. i. p. 202.

cases of malignant jaundice from primary suppurative hepatitis in multiple foci; and lastly, vi. cases of recovery.[*]

After this time it is impossible to separate the history of acute yellow atrophy and that of phosphorus poisoning; for in 1862 Ernst Wagner, finding that the chemists could detect no phosphorus in the bodies of those dying of undoubted poisoning by phosphorus, ventured upon the assertion that Rokitansky's and some of Wunderlich's cases of supposed acute atrophy were nothing but cases of phosphorus poisoning,[†] and in this opinion he has been supported by many, and the complete identity of these two processes has been asserted. Opinion in Germany is even now divided into two rival camps; one, with Liebermeister[‡] and Ossikovszky,[§] asserting that no distinction can be drawn between acute yellow atrophy, phosphorus poisoning, and yellow fever; the other, with Schultzen and Riess,[‖] and Winiwarter,[†] declaring that there exist certain means, both before and after death, for distinguishing between these differing states. The literature of this strife is almost entirely German, England and France taking but little part in the discussion.

Ætiology. It is agreed on all hands that acute yellow atrophy is one of the rarest diseases known to man. It seems likely that there is no other disease of equal intensity which at all comes up to it in rarity. A physician in one of the largest consulting practices in

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[*] Wunderlich, *Arch. der Heilkunde*, 1860. Bd. i. p. 210. Cf. *ibid.* 1863. Bd. iv. p. 145.

[†] E. Wagner, *ibid.* 1862. Jahrg. iii. p. 364.

[‡] Liebermeister, *Beiträge zur path. Anat. u. Klinik d. Leberkrankheiten*, Tübingen, 1864. p. 266.

[§] Ossikovszky, *Wien. med. Presse* 1870. No. 50. reported in Virchow and Hirsch's *Jahresb. f.* 1870. Bd. ii. p. 169.

[‖] Schultzen and Riess, *Annalen des Charité-Krankenhauses*, 1869. Bd. xv. p. 1.

[¶] Winiwarter, *Med. Jahrbb. herausgeg. von d. k.k. Gesell. d. AA. zu Wien.* 1872. p. 256.

London, assured me a few years ago that he had never seen one instance of this disease. At St. Bartholomew's, although I have watched the *post-mortem* examinations carefully, there has been only one case during the last nine years. Two others, indeed, were suspected before death; but in England the friends of the dead have the power of forbidding examinations after death; and thus the diagnosis remained unverified.

The sex of the patient has great influence as a cause of this disease. Frerichs collected 31 cases, and out of these, 9 were men, and 22 women.* These cases were all carefully selected, and none was admitted but those which Frerichs judged to be acute yellow atrophy κατ' ἐξοχήν. Lebert, on the other hand, being less careful in excluding doubtful cases, found that out of 72 instances, 44 were men and 28 women, a proportion of 11 to 7.† I have myself collected 100 cases of idiopathic acute yellow atrophy of the liver, excluding all in which the diagnosis was not verified after death by finding destruction of the liver cells, and disregarding all cases in which there was a suspicion of poisoning by phosphorus, alcohol, or the like.‡ Out of these 100 cases, 69 were women or girls. The remaining 31 were men or boys. These figures agree in general with those of Frerichs.

Then as to the age of the patient. There can be no doubt that the years of youth are those most open to attacks of this disease. Bamberger thinks that the age of 15 to 35 is that at which the greatest predisposition exists.§ According to Lebert one-eighth of all the cases was seen between the ages of 10 and 15; 32 out of his 63 fell between the ages of 15 and 25, that is, more than one half. Only one ninth of the cases fell between the 25th and 30th years. Frerichs came with his figures to a very similar result. Out of 31, six were seen from 10 to 20 years; 20, that is, nearly two-thirds of the whole, from 20 to 30 years; and 3, from 30 to 40. In my own 100 cases, I found 7 below the age of 5; none between 5 and 10; 4 between 10 and 14; 45 between 15 and 25; 31 between 25 and 35; 10 between 35 and 45; and 3 between 50 and 60; thus the opinions of three foregoing observers are in the more important points sustained.

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* Frerichs, *Klinik d. Leberkrankheiten*, Braunschweig, 1858. Bd. i. p. 243.

† Lebert, *Arch. f. path. Anat.* 1854. Bd. vii. p. 383.

‡ These figures were put together in the winter of 1876-77: but since that time several new cases have been met with or published, of which no use has been made in the numbers.

§ Bamberger, *Krankheiten des chylopoëtischen Systems*, Erlangen, 1864. 2te Auflage, p. 530.

In infancy and childhood there can be no doubt that acute yellow atrophy is rarely seen, and there are but meagre accounts of it in the books devoted to the diseases of childhood. Lebert, out of his 63 cases, collected only two before the age of 10 years. Felix von Niemeyer has ventured on the assertion that the disease is never seen in childhood;[*] and Bamberger seems to think it doubtful if the disease be ever seen under 10 years of age.[†] There is, however, strong evidence to contest this statement, as the following cases will show.

Loeschner, for example, has described a well-marked case in a boy three and a half years old.[‡] Dr. Tuckwell speaks of two undoubted cases, one, a boy aged 4 years and 10 months, and the other a girl aged 4 years and six months;[§] and Dr. Hilton Fagge has published the case of a boy, two and a half years old, whose delirium was thought at first to be due to belladonna poisoning; but after death the liver was found in a well-marked state of yellow atrophy, with the cells destroyed.* A like case in a boy of two and a quarter years has been described by Rehn, the examination after death and with the microscope being made by Perls.† Quite recently Senator has described a case in a child aged eight months.‡

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[*] F. von Niemeyer, *Text Book of Practical Medicine*, Humphreys and Hackley's Translation, London, 1870. Vol. i. p. 689.

[†] Bamberger, *loc. cit.*

[‡] Loeschner, Schmidt's *Jahrbb.* 1856. Bd. xci. p. 204.

[§] Henry M Tuckwell, *St. Bartholomew's Hospital Reports*, 1874. Vol. x. p. 39.

Politzer, indeed, describes a case in a new-born child. A little girl began to be jaundiced four days after birth. There was bloody vomit, and the stools were white with black points, due to altered blood corpuscles. The percussion dulness of the liver became small, especially over the left lobe; and the spleen increased in size. On the fifteenth day after birth, bleeding from the navel came on, then convulsions, and the child died eighteen days after birth. After death, blood was found extravasated in the meninges of the brain and cerebellum. Other hæmorrhages were also noticed, as into the pancreas; the kidneys were pale, but were not examined with the microscope. The liver was decreased in size, especially in the left lobe; and the cells were found destroyed, and a fatty detritus was seen under the microscope. The common, hepatic, and cystic ducts were free.§

At first sight it might appear to some that this case belongs to those fortunately rare, but very fatal, cases of umbilical hæmorrhage complicated with jaundice. The records of these cases show but very few observations upon the cells of the liver, so that it is not known if solution of the cells be at all a common event in these cases. A hæmorrhagic diathesis is also a very common complication; and especially common are hæmorrhages into the stomach and intestines. Thus there are several points in which acute yellow atrophy and umbilical hæmorrhage resemble each other. Unfortunately too, in this case of Politzer's, there was no examination with the microscope of the heart and kidneys. Nevertheless the combination of acute jaundice with solution of the liver cells is so important in a diagnostic point of view that I do not think we can refuse to class this case under the head of idiopathic yellow atrophy.

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* Hilton Fagge, *Trans. of the Pathological Society of London*, 1869. Vol. xx. p. 212.

† Rehn, *Berlin. klin. Wochenschrift*, 1875. p. 649.

‡ Senator, *Centralblatt f. d. med. Wiss.* 1878. p. 735.

§ Politzer, *Jahrbuch f. Kinderheilkunde*, 1860. Bd. iii. p. 40.

No unquestionable cases have as yet been published of acute yellow atrophy between the ages of 4½ and 10 years. It is a curious fact, but doubtless without any practical value.

Late in life there seems to be no disposition to acute yellow atrophy: cases above 50 are very rare. Lebert found only 3 above the age of 45 and Frerichs only 2 between 40 and 60. I have only been able to meet with 3 undoubted cases. One is a case of Dr. Budd's, in which the age of the patient, a lascar, is said to be between 50 and 60 and is therefore open to some question;[*] the second, a woman aged 55, recorded by Spengler;[†] and a third, a man aged 53, spoken of by Liebermeister.[‡]

Pregnancy is a most important predisposing cause. Perhaps it is the best established of any. Out of 31 cases collected by Frerichs 22 were women, and 11 of these women were pregnant:[§] Bamberger says that out of the 7 cases altogether which he has seen, 3 were in pregnant women.[‖] Out of the 69 cases in women which I have collected, pregnancy was present in 25; in 3 others delivery preceded the jaundice by a few months. In the other cases pregnancy is not spoken of, or it is ex-

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[*] Budd, *On Diseases of the Liver*, London, 1857. Third ed. p. 251.

[†] Spengler, *Arch. f. path. Anat.* 1854. Bd. vi. p. 129.

[‡] Liebermeister, *Beiträge zur path. Anat. u. Klinik d. Leberkrankheiten*, Tübingen, 1864. p. 189.

[§] Frerichs, *loc. cit.*

[‖] Bamberger, *loc. cit*

pressly denied on *post-mortem* evidence. These figures, it will be seen, are somewhat lower than those of Frerichs; but they serve to confirm the general correctness of his observations. Frerichs remarks with truth that acute yellow atrophy is most commonly seen from the third to the sixth months. Out of 22 cases in which the time of the pregnancy is given I found the following proportion :

MONTHS OF PREGNANCY	4	5	6	7	8	9
NUMBER OF CASES	3	4	7	4	1	3

The greatest number was thus seen in the sixth month: three in the fourth, and four in the fifth, and seventh ; none before the third month.

Pregnancy and suckling seem to have a remarkable influence upon the glands, especially the liver and kidneys. Virchow in 1848 drew attention to the cloudy swelling of the liver and kidneys in pregnancy.[*] The albuminuria which accompanies pregnancy has long been known, and sometimes explained by the pressure of the uterus upon the renal veins, just as the jaundice of pregnancy is explained by the pressure of the uterus upon the gall ducts. But this parenchymatous degeneration of the cells of the liver in pregnancy becomes of very great importance, as Frerichs has pointed out, when taken in connexion with the tendency of pregnant women to acute yellow atrophy.

Meissner also pointed out that the livers of hens, in the summer, while they were laying, contained a large quantity of fat, while the livers of cocks contained scarcely any. In the winter, when no eggs were laid, the livers of hens and of cocks contained a like quantity of fat. But in all hens who were laying eggs, the quantity of fat was enormous.[†] Cornil and Ranvier say

[*] Virchow, *Gesam. Abhandl.* Hamm, 1862. Zweite Ausgabe, p. 778.

[†] Meissner, *Zeitschrift f. rat. Med.* 1869. iiite Reihe, Bd. xxxv. Bericht, p. 209.

that the liver cells of all female animals giving suck are surcharged with an excess of fat,[*] and Sinéty, following apparently the suggestion of Ranvier's, found the liver fatty in several kinds of brutes, and in women, as soon as lactation was set up. But it is independent of gestation, and in one observation, Sinéty did not find the kidneys or muscles fatty. The fat was placed around the hepatic vein of the lobule, and not in the periphery.[†] J. C. Lehmann speaks of the parenchymatous degenerations seen in pregnancy as if they were well known; he says they reach their height at the end of gestation.[‡]

In Lebert's collection of recorded cases it was thought that the season of the year had some influence: during the milder months, April, May, September, and October, very few cases were seen. The greatest number was seen in November, December, January, and February; and again in June, July and August: so that the extremes of heat and cold are alike favourable to the disease.

In my own 100 cases the season of the year has not always been given by the author, or rather in the abstracts which I have seen. But in the greater number the time of year is stated. I have preferred to arrange the cases according to the month in which the patient died as the *prodroma* in some cases last for weeks and even months. The mortality seems tolerably evenly divided amongst the months of the year, with the exception of April.

January . .	9	July . . .	7
February .	10	August . .	6
March . .	6	September .	7
April . .	2	October . .	9
May . . .	9	November .	8
June . . .	7	December .	7

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[*] Cornil and Ranvier, *Manuel d'Histologie path.* Paris, 1869, p. 53.

[†] L. de Sinéty, *de l'état du foie chez les femelles en lactation*, Paris, 1873. The references which Sinéty gives of earlier observations admit of explanation of the fatty liver being caused by disease, not by suckling.

[‡] J. C. Lehmann, Schmidt's *Jahrbb.* 1868. Bd. cxxxix. p. 239.

But, in truth, the number is not large enough for any good information to be drawn from this collection of figures.

The other causes of acute yellow atrophy are very obscure, and much doubt may be reasonably entertained if the statements of authors will hereafter be confirmed.

One of the first causes of acute yellow atrophy spoken of by Lebert, and endorsed by Frerichs, is the influence of the emotions, especially of the depressing emotions. Out of Lebert's 72 cases, he counted 13 as due to this cause, and speaks of the cases of Vercellonus and Morgagni, already quoted, as cases in point. Out of my own carefully chosen 100 cases, I found only 16 in which the presence of some depressing emotion is spoken of, 13 of these, as might be looked for, were women, and in 7 of these, that is, about one half, the depressing emotion was complicated by pregnancy; in one case, anger and habits of drink were combined, and in another, unhappiness and syphilis. So that only in four of the women was the influence of depressing emotion uncomplicated. In the three cases of men, one man was a Frenchman, aged 22, a prisoner in the hands of the Germans in the war of 1870, who had chancres on his foreskin as well, and who may be set down as miserable from his ill fortune, although nothing is said about this in the report.[*] A second case is one of Vallin's; a young soldier, of a remarkable soberness, but always melancholy from certain family troubles;[†] and the third is a case of Chaumel's; in which a man of 29, given to no excess, was troubled with great distress of mind and thoughts of suicide.[‡] This case is also complicated by chronic copper poisoning and erysipelas.

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[*] v. Krafft-Ebing, Virchow and Hirsch's *Jahresbericht f.* 1871. Bd. ii. p. 161.

[†] Vallin, *Gaz. hebd.* 1867. t. iv. p. 487.

[‡] Chaumel, *Gaz. des hôp.* 1863. p. 309.

For a more prolonged discussion of emotion as a cause, see the end of the chapter on the Pathology of Acute Yellow Atrophy.

Persons of irregular life, habitually committing excesses of all kinds are thought by Lebert to be predisposed to this disease, especially prostitutes. And here it is hard to distinguish between the excesses *in Venere*, in drunkenness, and in misery which the profession of a *puella publica* bring upon the unfortunate persons who exercise it. For nearly all of these three must press heavily upon them. Only five out of the 69 women were prostitutes. Eight of the 100 cases, counting men and women, were syphilitic. Whether this represent a larger proportion than is common among the whole of the population may very well be doubted. In some of the cases, however, the inoculation with syphilis seems to have been the starting point of the disorder, as in Mr. Robinson's,[*] Dr. Andrew's[†] and Dr. Goodridge's[‡] cases. In these the action of the syphilitic virus suggests a comparison with the action of certain poisons, phosphorus and the like, especially as the secondary stage of syphilis, or its treatment, seems to dispose a person to become jaundiced. (See Chapter xxvii. *Icterus Syphiliticus.*)

The relations of the poisons, phosphorus, alcohol, antimony and arsenic, mercury, and the like, to acute yellow atrophy are so important that it will be best not to speak of them here, but devote a separate chapter to their complete discussion. (See Chapter xxiv. and the two following.)

One very noteworthy point in this obscure disease is its appearance amongst kinsfolk, brothers and sisters living under the same roof. Griffin describes a family of this sort. A girl, twenty years old, was found at the point of death. Two or three days before death she had vomited and become jaundiced. Soon after she became comatose and died. Three weeks after, her sister began to suffer from vomiting and jaundice. She was comatose when seen by Griffin, but recovered after active purgation. Soon after, a brother, aged 13, was attacked with the same symptoms and died before the end of the third day. At the end of a few months another brother, aged 11, began to vomit, and was jaundiced. He was actively purged, but notwithstanding this, he became comatose. After about 24 hours of coma, he began to wake up, and gradually recovered, after suffering a relapse.*

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[*] Robinson, *Trans. of the Path. Soc. of Lond.* 1865. Vol. xvi. p. 152.

[†] Andrew, *ibid.* 1866. Vol. xvii. p. 158.

[‡] Goodridge, *Brit. Med. Journal*, 1871. Vol. i. p. 609.

There is a like set of cases, also from Ireland, recorded by Graves, the notes being sent to him by Dr. Hanlon of Portarlington.† A girl aged 17, in good health, was suddenly seized with vomiting and jaundice. On the fifth day of the illness she had headache, intolerance of light, and vomiting of coffee-ground matter. Soon after she fell into imperfect coma, then into convulsions, and died on the morning of the sixth day, July 28, 1840. In March 1841, the sister, aged 11, fell ill with a feverish cold; on the third day of the disease she became jaundiced, and died on the fourth, after vomiting black matter, and passing into a state of insensibility varied with convulsions. The examination after death showed the liver to be natural in size, of dull yellow, with several dark spots the size of half a crown; consistence less than usual. The cut surface was minutely granular and of a very peculiar crimson orange colour. In the June of the same year, another sister, aged 8, fell ill. She became jaundiced and vomited. On the second day there were some headache, intolerance of light, and restlessness, but these were the only nervous symptoms noticed, and on the third day she began to recover, and at the time of Dr. Hanlon's report was quite well.

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* Griffin, *London Med. Gaz.* 1834. Vol. xiii. p. 801.

† Hanlon, reported by Graves, *Clinical Lectures*, Dublin, 1864. p. 634.

In these cases it is worthy of note that some of the family attacked by jaundice recovered, and others died. The fatal cases seem as well marked as any of the others reported so early, and in which therefore no microscope was used for diagnosis. A well-marked instance of acute yellow atrophy with jaundice in other members of the family came under my notice some years ago. A little girl 10 years old, was brought by her sister to me at St. Bartholomew's Hospital on May 2nd, 1870. She was then simply jaundiced, and the jaundice continued to grow deeper till May 19th when the sister of the child came and told me that delirium had set in early that morning. Admitted at once into the hospital, nothing was found wrong with the liver; her furious delirium passed into coma, and she died at 4 in the afternoon on May 20th. After death, the liver was of natural size; on examining it with the microscope, the left lobe showed no longer any liver cells, but a dark granular detritus; however, in the right lobe, a few cells still remained. There was fatty degeneration of the glands of the stomach and of the kidneys, but the fibres of the heart were untouched. In February, 1871, a brother of this patient, aged 19, was admitted into St. Bartholomew's deeply jaundiced, and partly delirious. He had been ill since the October of last year. A week before admission, he had been delirious for two days. He died five days after admission, the same symptoms continuing; and at the last coffee-ground matter being vomited. The friends forbade the body to be opened, but a part of the liver was secured by means of Duchenne's hook, and examined under the microscope. The hepatic cells were well preserved, but filled with fatty and minute granules, not, however, in sufficient quantity to obscure the nucleus.* It may be noted, however, that the parts of the liver in which the process was most advanced would probably not be brought up by this means.

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* Dyce Duckworth and J. Wickham Legg, *St. Bartholomew's Hospital Reports*, 1871. Vol. vii. p. 208.

Two sisters had likewise been jaundiced, but had recovered; and here there is a remarkable likeness to Griffin's and Hanlon's cases. Frerichs doubts if Griffin's and Hanlon's cases can be classed under acute yellow atrophy,* but there can be no doubt that in my own case of the little girl, if not in Dr. Duckworth's case of the brother, acute yellow atrophy was present. They must, I think, be studied alongside of those cases of epidemic jaundice, in which the greater number of those attacked recover, but one, two, or three fall victims to a disease which, in clinical features at all events, shows a great analogy to acute yellow atrophy.† For instance, in one of the first epidemics recorded at length, Mende remarks that all recovered save one young man, who died with symptoms like those of acute yellow atrophy, delirium, coma, and hæmorrhagic diathesis. There was no examination after death.‡ Then in other epidemics the pregnant women only have died with symptoms of *icterus gravis*, while those not pregnant, and men, recovered without trouble.§

The account which Carville has given of an epidemic of jaundice in a prison has already been spoken of under the head of *icterus epidemius*.‖ Here a singularly rare and valuable opportunity of studying after death the phænomena of what Carville calls *ictère grave épidémique* has been lost, the use of the microscope having been altogether neglected. It was most important, that the state of liver cells, of the epithelium of the kidneys, the glands of the stomach, and fibres of the heart, should be established before the name *icterus gravis* could be assigned to the cases brought forward by Carville. The report remains of much interest; which would have been greatly heightened if the state of the organs after death had been accurately known. An epidemic on a smaller scale, and with a like disregard of the microscope, has been described by Arnould and Coyne. The naked eye appearances of the organs and the symptoms during life were all those of *icterus gravis**.

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* Frerichs, *op. cit.* Bd. i. p. 245.

† See the foregoing chapter of this work, on *icterus epidemius*, p. 406.

‡ Mende, Hufeland's *Journal*, 1810, Bd. xxxi. Stück viii. p. 93.

§ Klingelhoeffer, *Berlin. klin. Wochenschrift*, 1876. p. 76. Saint Vel, *Gazette des Hôp.* 1862. p. 538. Kercksig, Hufeland's *Journal*, 1799. Bd. vii. Stuck iii. p. 94 and several others.

‖ Carville, *Arch. gén. de Méd.* 1864. Vol. ii. p. 129.

* Arnould and Coyne, *Gaz. méd. de Paris*, 1878. p. 114.

CHAPTER XX.

THE SYMPTOMS OF ACUTE YELLOW ATROPHY.

BEFORE entering more into detail, it may be well to give a short account of the more prominent symptoms of this disorder, so that the reader may have beforehand some insight into the course of the symptoms.

The disease begins either suddenly without warning, or else with the symptoms of an ordinary gastric catarrh. After this has lasted a certain time, a jaundice appears, with no specific characters, but apparently as simple as the gastric catarrh. In the midst of this state, which gives no warning of what is about to follow, delirium, coma, or convulsions, suddenly set in; hæmorrhages take place from the nose and mouth; there is vomiting of a black matter, and the stools, colourless before, become black from the presence of blood. The liver decreases in size as told by percussion, and the spleen enlarges. The pupils are dilated, the pulse becomes quick, and the temperature often is raised. Death commonly takes place in from 12 to 48 hours after the nervous symptoms began.

Prodroma. It was long ago pointed out by Ozanam that there are two ways in which acute yellow atrophy may develope itself: one, in which grave symptoms exist from the first; and the other, in which the course of the disease is insidious,* symptoms, which in themselves cause no alarm, preceding the jaundice and severe phænomena.

The most common forerunner of the jaundice is an acute gastric catarrh. If the cases of pregnancy be excluded in which vomiting, nausea, and the like are exceedingly common, symptoms of gastric disturbance will be found in about one half of the remainder of all cases. These symptoms have a great uniformity. They are vomiting or nausea, loss of appetite, pain in the epigastrium, headache, malaise, and sense of weakness, eructations and a bad taste in the mouth, diarrhœa or constipation. The length of time which these symptoms may last is very various. The most is from a week to ten days or a fortnight, but in many it is longer, and in some covers a space of months.[*] In Buhl's case the man had intermitting gastric attacks for five years before the jaundice set in.[†]

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* Ozanam, *De la forme grave de l'ictère essentiel*, Thèse de Paris, 1849. p. 15.

In the remainder of the cases in which there existed some disturbance of health before the jaundice arose, gastro-intestinal symptoms were seen in a few.

In Traube's cases a painless diarrhœa lasting four weeks preceded the jaundice in one, and in another a too great eating of fruit.[‡] An excess in mushrooms is spoken of by Hecker, the mushrooms being thought to be poisonous.[§] In another case vomiting set in after the eating of pease-soup. In Leichtenstern's case, rendered doubtful by the recovery of the patient, there was hæmatemesis five weeks before the jaundice, and for many years there were symptoms of ulcer of the stomach and of chlorosis.[||] In one of Homans' cases, the patient, a sailor, eat abundantly of green apples, apparently after the jaundice had come on.[¶]

Setting aside the cases with acute gastric catarrh, the majority of the remaining cases show no *prodroma* whatever, the jaundice setting in without any warn-

[*] Homans, *American Journal of the Med. Sciences*, 1868. Vol. lvi. p. 53. von Plazer, Schmidt's *Jahrbb.* 1860. Bd. cvii. p. 35.

[†] Buhl, *Zeitschrift f. rat. Med.* 1854. Bd. iv. N. F. p. 351.

[‡] Traube, *Gesam. Beiträge*, Berlin, 1871. Bd. ii. p. 815.

[§] Hecker, *Monatsschrift f. Geburtskunde*, 1863, Bd. xxi. p. 210.

[||] Leichtenstern, *Zeitschrift f. rat. Med.* 1869, iii. Reihe, Bd. xxxvi. p. 241.

[¶] Homans, *American Journal of the Medical Sciences*, 1868, Vol. lvi. p. 60.

ing being recorded. It must not be too readily assumed, however, that because no gastric symptoms are recorded that therefore none existed. The existence of a slight *embarras gastrique* may readily be overlooked, if not specially sought for. Amongst the cases without *prodroma* must be included those cases in which the patient was already comatose at the time when he first came under observation and of whom no information as to foregoing health could be had.

Jaundice. This symptom is never[*] absent, however late in the disease it may come on, or slight it may be. It varies much in degree of intensity, being sometimes very slight, at other times deep. As a rule the patient is markedly, but not intensely, jaundiced. When first the jaundice is noted, it is stated by Frerichs to be seen only on the upper half of the body;[†] and in Hecker's case it apparently never spread further;[‡] but Hecker's is one of the most rapid cases on record. The jaundice may only be noticed after death.[§] There are some facts which point to the assumption that the intensity of the jaundice depends on the length of time which this symptom has lasted.

When the jaundice first appears there is commonly no means by which it can be separated from an ordinary simple jaundice. The pulse is natural in its number of beats, or below the usual standard: the temperature natural or below the normal. During this period of the disease the urine appears to be high-coloured and bilious-looking, but I have not found any records of a chemical examination. The stools at this time of the disease are most commonly free from bile; they are colourless, grey or white; or they may still show a slight brown or yellow colour, or be particoloured.

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[*] Bamberger, (*Khten. d. chyl. Syst.* Erlangen, 1864, p. 532, note,) thinks the absence of jaundice not to be impossible. He quotes the case of a parturient woman who had maniacal attacks with slight spasms of the voluntary muscles, and died thirty-eight hours after delivery. Neither before nor after death was jaundice present. The liver showed a high degree of acute yellow atrophy: only here and there could liver cells be seen.

[†] Frerichs, *Klinik d. Leberkrankheiten*, Braunschweig, 1858, Bd. i. p. 224.

[‡] Hecker, *Monatsschrift f. Geburtskunde*, 1863, Bd. xxi. p. 210.

[§] Stehberger, *Arch. d. Heilkunde*, 1866, Bd. vii. p. 281.

The late Dr. Murchison stated that the stools in acute yellow atrophy "contain plenty of bile" and he introduced this disease amongst those kinds of jaundice in which no obstruction to the ducts is present.[*] I think this statement may be due to the fact that in Dr. Murchison's own case[†] the motions were said to be green, and everyone is disposed in describing a disease to rely upon his own experience. Still this statement is not in accordance with the experience of others.[‡] There are 39 cases out of a hundred in which the colour of the stools was grey. And in 45 the colour is not noted.

The want of colour is confirmed by such authors as Rokitansky,[§] Frerichs,[||] Lebert,[¶] Leyden,[**] and others. In 16 cases of the 100 cases which I have collected, the stools were certainly coloured; but attention should be given to the kind of colour which they presented, and also to the time of the disease at which the observations were made. For example, in Frerichs' first case, the stools were, at the beginning of the disorder, dark, but later became clay-coloured.[††] Out of the cases there are only three in which the colour of the stools was bilious throughout the disease, or after death: in Concato's case the stools were greenish throughout,[§§]

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[*] Murchison, *Clinical Lectures on Diseases of the Liver*, London, 1868. p. 395.

[†] *Op. cit.* p. 236.

[‡] Morgagni, one of the earliest to note this disorder, says that the stools were uncoloured. (*de Sedibus, etc.* Ep. xxxvii. § 2.)

[§] Rokitansky, *Lehrb. d. path. Anat.* Wien 1861. 3te Auf. Bd. iii. p. 270.

[||] Frerichs, *op. cit.* Bd. i. p. 228.

[¶] Lebert, *Arch. f. path. Anat.* 1854. Bd. vii. p. 371. In 20 cases, the stools were coloured in 7, and uncoloured, white, or grey, in 13.

[**] Leyden, *Beiträge zur Path. des Icterus*, Berlin, 1866. p. 164.

[††] Frerichs, *op. cit.* Bd. i. p. 210.

[§§] Concato, *Annali universali di Medicina*, 1861. Vol. clxxvii. p. 7.

and in Braun's[*] and Standthartner's[†] cases the contents of the intestine were after death found to be bilious. In Dr. Murchison's case already spoken of, the stools were said to be green before the patient was brought to the Hospital; in Homans' first case the stools were yellow after calomel had been given;[‡] and in von Krafft-Ebing's case the first stool passed was brown, the second one lighter in colour.[§] Waldeyer's case is rather hard to explain. The stools a fortnight or more before death were grey yellow: four days before death they became natural in colour, and the urine brighter; yet after death a white plug of mucus was found in the *papilla duodenalis*, and the hepatic duct quite pale, a very slight yellow colour in the smaller ducts. The contents of the duodenum were scarcely tinged yellow.[||]

In the other cases the stools are said to be dark or black; and as the time at which they were noted was late in the disease after the nervous symptoms had appeared, there can be no doubt as to the interpretation of their colour. It will be shown that hæmorrhages into the stomach and intestinal tract are almost an essential part of this disease; and it is well known that blood gives a black colour to the stools. In some cases it is noted that part of the fæces was coloured black, part grey.[¶]

Another point worthy of notice is, that in a very large number of cases, the bile ducts are reported to be free from colour, or at the most to hold a little yellowish mucus. That this was the case in one instance, at all events, Dr. Murchison himself testifies. If, then, the green colour of the stools be due to the presence of bile, how did the bile pass from the liver into the duodenum without staining the mucous membrane of the ducts? It can scarcely be suggested that the bile was secreted by the mucous membrane of the intestines instead of the liver.

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[*] Braun, *Allg. Wien. med. Zeitung*, 1863. p. 281.

[†] Standthartner, *Zeitschrift d. kk. Gesellschaft d. Aerzte zu Wien*, 1858. p. 785.

[‡] Homans, *loc. cit.*

[§] Von Krafft-Ebing, Virchow and Hirsch's *Jahresbericht f.* 1871. Bd. ii. p. 161.

[||] Waldeyer, *Arch. f. path. Anat.* 1868. Bd. xliii. pp. 534 and 535. It is stated that the common and cystic ducts were coloured intensely yellow: this is probably a *post-mortem* appearance caused by the pressure used to squeeze out the plug from the papilla.

[¶] In Karl Kétli's case of *icterus gravis catarrhalis*, the stools were first grey, then brown; and this brown colour was found to be due to the blood pigment. (*Wien. med. Wochenschrift*, 1878. p. 137.)

To account for the particoloured appearance of the stools, Dr. Hilton Fagge suggests that as in acute yellow atrophy the whole of the gland is not affected uniformly, but some parts are attacked earlier than others, so bile may continue to be poured into the ducts by those parts of the liver which are less affected.[*]

It may be asserted, then, that in acute yellow atrophy up to the appearance of the hæmorrhagic diathesis, the stools are, as a rule, free from colour. After the hæmorrhages have set in, the stools often become black and tarry, though this is by no means always so; and that in some rare cases the stools show a green or bilious appearance, though the source of this colour still remains unknown.

The length of time which the jaundice lasts before grave symptoms set in is very variable. In typical cases it lasts from ten days to three weeks, but it may be much longer or much shorter. Thus in one of Winiwarter's cases, in which it must be owned the diagnosis is not altogether free from doubt, the nervous symptoms set in before the jaundice appeared.[†] The shortest intervals between the arrival of jaundice and the appearance of nervous symptoms seem to me on a careful comparison of the cases, to be seen in pregnant women. Here indeed the whole disease runs a very rapid course.

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[*] Hilton Fagge, *Guy's Hospital Reports*, 1875. Vol. xx. Third series, p. 159.

[†] Winiwarter, Stricker's *Med. Jahrbb. herausgeg. v. d. kk. Gesellschaft d. AA. zu Wien*, 1872. p. 258.

Frerichs seems to think that the jaundice and the nervous symptoms set in, as a rule, at the same time.* This is an opinion which cannot now be maintained. Setting aside pregnant women, it is very rare for the jaundice not to precede the nervous symptoms by some hours or days.

The jaundice, on the other hand, may last several weeks or months before grave symptoms be seen. In Trost's case, the woman was jaundiced 3 months before she lost consciousness.† In Picot's case the jaundice lasted apparently from the end of April to the beginning of August.‡ In one of Fritz' cases, the jaundice appeared in March, and the woman's manner was first noticed to be curious on May 8th. Delirium set in the same night.§

The Grave Symptoms. These may be conveniently discussed under certain heads: i. the nervous symptoms; ii. the hæmorrhagic diathesis; iii. the rise in temperature and pulse; iv. the decrease in size of the percussion dulness of the liver, and the increase in size of the spleen; v. the less prominent and accidental symptoms; vi. and lastly, the state of the blood and of the urine will be spoken of.

i. The nervous symptoms are commonly those which first arouse attention, and make the bystanders aware that the disorder is serious.

In a case of simple jaundice, dilatation of the pupils should never escape notice. This is very often one of the first appearances of the nervous phænomena and should at once set the physician on the alert. Ozanam noticed this premonitory sign, and pointed out its importance as a warning of what was to come.‖

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* Frerichs, *op. cit.* Bd. i. p. 230.

† Trost, Schmidt's *Jahrbb.* 1860. Bd. cv. p. 185.

‡ Picot, *Journal de l'anatomie*, 1872. p. 246.

§ Fritz, *Gaz. des Hôp.* 1863. p. 81.

‖ Ozanam, *De la forme grave de l'ictère essentiel*, Thèse de Paris, 1849, p. 33.

I consider that in these cases it is most necessary to watch the state of the pupil, although Frerichs says it is not constantly dilated and that very rarely he has seen it contracted.* In the same manner Frerichs says that the nervous symptoms attract attention earlier than the jaundice which is at that time only noticeable in the conjunctivæ and alæ nasi.† I have already pointed out that in the majority of cases the jaundice precedes the nervous symptoms by days, if not weeks. It is but seldom that the jaundice and nervous symptoms appear at the same moment.

Other warnings, besides dilatation of the pupils, may be given. Headache, sometimes very violent; rigors; extreme restlessness; jactitation; or a confused manner; but with these last the boundary between mere warnings and serious symptoms has been passed, and the attention of even inobservant persons will be aroused.

The strongly-marked symptoms now appear. Ozanam has divided them into two periods, first of excitation, then of collapse.‡ Had he divided the symptoms into two kinds, the arrangement would have been better, for the signs of excitement do not always go before those of collapse; and convulsions are often seen in the midst of coma.

In a large number of cases no warning whatever has been seen before the alarming symptoms began. The patients have been suddenly seized with delirium or become insensible. In one of Bamberger's cases the

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In one of Dr. Hilton Fagge's cases (*Trans. of the Path. Soc. of Lond.* 1869, Vol. xx. p. 212) the dilatation of the pupils was so enormous, and the delirium of the child so marked, that it was thought by the surgeon in attendance that the case was one of belladonna poisoning.

* Frerichs, *op. cit.* Bd. i. p. 230. Bamberger says it is usually first contracted (*op. cit.* p. 534) a statement with which I can scarcely agree. In Budd's case (*On Diseases of the Liver*, London, 1857, p. 251) the pupils were much contracted, but then a box of opium was found on the patient.

† Frerichs, *op. cit.* Bd. i. p. 230. This statement is quite at variance with another at p. 224.

‡ Ozanam, *op. cit.* p. 16.

patient suddenly fell on the stairs, and began to be delirious.* Or convulsions may be the first sign.

In some cases the period of excitement is entirely absent, and the patient from sleepiness passes into coma, from which he never awakes. Materials for a numerical treatment of these cases are not so abundant as might at first be thought, for as much as the nervous symptoms are often the first to attract serious attention, and the patient only comes under medical observation when coma and delirium, or a like incapacity for answering questions, have been established.

One of the first symptoms noticed is often a drowsiness, lasting for a few hours, when it is broken by a maniacal outbreak of delirium. In the delirium, the patients are exceedingly violent; they strike at and bite the bystanders. After the access of delirium, the the patients fall again into the drowsy state in which the attack found them. By degrees, the coma becomes more and more deep without any delirium. The patient can no longer be awaked, and death follows after a longer or a shorter interval.

It is impossible to point out all the different forms which the three chief nervous symptoms may take, or the order in which they appear or follow each other. Thus the delirium may be of the slightest kind, the patient not giving perfectly correct answers to questions; and from this it may pass through all degrees up to the most furious madness, so that some observers speak of mania, and the Germans describe the attacks as *Wuthanfälle*. Then the delirium, when marked, may be of exceedingly short duration. In one of Traube's cases, the patient had an attack of furious delirium for an hour only,† followed by sleep and a second attack of delirium for half an hour. Or on the other hand the delirium may last until the patient's death. In like manner, the coma may be marked merely by a slight drowsiness, or become so deep as to be called a *carus*. So also the convulsions: they may show themselves by slight involuntary contractions of the muscles, or be expressed by strong epileptic seizures, or tetanus. Then as to the order in which they are seen; it is the rule for the delirium to precede the coma, and the convulsions to come on during the insensibility. But in some cases the coma appears first, and the attacks of delirium break into the dreamy and unconscious state of the patient. Or convulsions may be seen early in this stage at the same time as the delirium, instead of appearing only when coma has set in.

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* Bamberger, *Verhandlungen der phys.-med. Gesellschaft in Würzburg*, 1858, Bd. viii. p. 269.

†, Traube, *Ges. Beiträge*, Berlin, 1871, Bd. ii. p. 815.

Out of a hundred cases of acute yellow atrophy, verified by finding the liver cells dissolved after death, 76 had suffered from coma, 59 from delirium, and 32 from convulsions. So that of the chief nervous symptoms, coma is the most, and convulsions the least, common.

Of the nervous symptoms, delirium and coma are those most commonly associated together. Out of the 100 cases, delirium and coma were noticed, and spoken of as being present together, at different times perhaps, in 49, nearly one half. I believe that in reality this number is too low, and that delirium is present in many cases in which it has not been noted. Many of the cases only come under observation when coma has been fully established, and the bystanders often can give no good account of the state of the patient before the coma set in.

Coma alone is spoken of in about 15 cases of the 100, and delirium alone in 7. Coma without delirium seems to be especially common in parturient women.

It is, however, very rare for convulsions to be seen alone without coma or delirium. Perhaps the only case in which this may have happened is Morand's. The patient suffered from attacks of emprosthotonos and opisthotonos for a few hours before death; at the end there was "*perte absolue de connaissance.*"[*]

In the majority of cases it is simply said that convulsions were present, without any minuter description. In others, however, tetanus is spoken of, and in others distinct attacks of emprosthotonos, opisthotonos, and trismus, are declared to have been seen. Concato speaks of "epilepsy" in his description,[†] and many authors have seen a tremor in the muscles or fibrillary contractions.[‡] In Steiner's case, a boy of ten, strabismus was noted as well as tetanus.[§]

And in a child aged one year and three quarters there were noticed only convulsions of the upper limbs and of the jaws.[‖] Indeed convulsive movements of the muscles of the head and upper limbs are more commonly noted than any other. In Dr. Wadham's case there were twitchings of the left side only,[¶] and the contractions of the muscles are not uncommonly limited to one set as well.

Hiccup, a spasm of the diaphragm, is noted in a good proportion of cases, and may cause much inconvenience and even pain to the patient.

Of the 10 cases on record of acute yellow atrophy in children, convulsions were present in 7, and not mentioned in 3. This exactly reverses the proportion in the general body of cases taken from all ages; for out of 100 of these, convulsions were present in only 30. The general proneness of children to convulsions is doubtless the reason for the high proportion of convulsive attacks seen in these cases.

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[*] Morand, *Gaz. d. Hôp.* 1873, p. 154.

[†] Concato, *Annali universali di Medicina*, 1861. Vol. clxxvii. p. 14.

[‡] Sotti, *Gazzetta medica Italiana, Provincie Venete*, 1872, anno xv. no. 18. I have not verified this.

[§] Steiner, *Jahrb. f. Kinderheilk.* 1871, Bd. iv. N. F. p. 428.

[‖] *Jahrb. f. Kinderheilkunde*, 1859, Bd. ii. p. 42.

[¶] Wadham, *Lancet*, 1872, Vol. i. p. 288.

In some few cases, a sort of aphasia is seen. In one of Traube's, the man, when asked what his trade was, answered: "a saddler," a perfectly correct answer. But when asked his age, he again answered: "a saddler" and so on to other questions.[*] So in Picot's case, besides blindness, there was what he calls *une véritable paralysie de l'intelligence.* The patient in answer to questions replied with trouble, often repeating the same word a great number of times, with the same accent and tone.[†] In Fritz' case, the woman, during a complete coma, said only one thing: *Est il possible?*[‡] The same thing has been noticed in one or two other cases.

Blindness was seen in Rehn's case towards the end of life,[§] as well as in Picot's. It is well to note this as Traube has denied that it is ever seen.

In some cases an increased sensibility of the skin, not merely over the belly, but all over the body has been noticed. Grinding of the teeth, screaming, and spitting are very commonly seen.

With the accession of the nervous symptoms, power over the sphincters of the bladder and rectum is commonly lost, and the stools and urine pass without the knowledge of the patient. Sometimes the opposite takes place, and the secretions are retained, and mechanical means have to be used for their removal.

Nervous symptoms have long been noted as essential parts of acute yellow atrophy. Lebert in his cases found that nervous symptoms of some sort were present in 64 out of 72 cases, and in 51 of these, delirium, coma, or convulsions were present.[*] Liebermeister considers this too low an estimate. Out of his 115 cases there were 101 in which there were severe nervous symptoms; but in the remaining 14, there are several cases in which it is expressly stated that there were no nervous symptoms, proof, thinks Liebermeister, that they are not essential to acute yellow atrophy.[†] Frerichs, however, says that they are absent in no case, and are characteristic symptoms.[‡] Bamberger is also of the same opinion,[§] and I must own that I am inclined myself to think them essential parts of the disease.

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[*] Traube, *Gesam. Beiträge*, Berlin, 1871, Bd. ii. p. 826.

[†] Picot, *Journal de l'Anatomie et de la Physiologie*, 1872, p. 247.

[‡] Fritz, *Gaz. d. Hôp.* 1863, p. 81. Cf. Morgagni (*de sedibus, etc.* Ep. xxxvii. § 4.) The young man in the midst of coma only called out: "Oh facinus indignum."

[§] Rehn, *Berliner klin. Wochenschrift*, 1875, p. 649.

Excluding all cases in which the liver cells were not found destroyed after death, I have been able to discover only six cases in which there is no precise mention of nervous symptoms. One of the first of these is Dr. Handfield Jones' case. There is certainly nothing in the clinical account about delirium; but shortly before death an attack of erysipelas of the face came on, and it is not uncommon in this disorder to have delirium. Yet nothing is said on this point.[‖] In Buhl's case, the patient, after losing a quantity of blood by the mouth, anus, and urethra, became collapsed, and the collapse is said to have been a sort of apparent death.[¶] In Prof. Ogston's case, no nervous symptoms were noticed, but the patient does not seem to have been watched by the surgeon in attendance up to the last.[**] And in Chaumel's case, the diagnosis of which is open to some doubt whether it were not a pyæmia, though there were no distinct nervous symptoms, yet the patient did not answer questions aright, and at the same time did not seem to feel the pain of cuts made to let pus out.[*] Also in Waldeyer's case there is no mention of nervous symptoms even at the last.[†] This is one of those cases which stand on the border land between acute yellow atrophy and cirrhosis. There were present ascites and œdema of the feet, but no hæmorrhages were noticed either before or after death. In Stehberger's case only is it expressly said that the woman retained consciousness up to the moment of death.[‡] It was one of those exceedingly rapid cases in which death quickly followed abortion, and the jaundice was only noticed after death. The immediate cause of death was flooding.

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[*] Lebert, *Arch. f. path. Anat.* 1854, Bd. vii. p. 372.

[†] Liebermeister, *Beiträge zur path. Anat. und Klinik d. Leberkrankheiten*, Tübingen, 1864, p. 254.

[‡] Frerichs, *op. cit.* Bd. i. p. 229.

[§] Bamberger, *Khten. d. chylopoët. Syst.* Erlang. 1864, p. 533.

[‖] Handfield Jones, *Lond. Med. Gaz.* 1847, N.S. Vol. v. p. 1145.

[¶] Buhl, *Zeitschrift f. rat. Med.* 1854, N.F. Bd. iv. p. 352. "Der Collapsus darauf glich einer Art Scheintod."

[**] Ogston, *Brit. Med. Journal*, 1873, Vol. i. p. 57.

There is only one case, therefore, of these six, in which nervous symptoms can be expressly excluded. And this case happened in a women rapidly dying after a premature delivery.[§]

The nervous symptoms may last but a few hours, as in some of the parturient women, or the disease may run on for several days or even for a week. In Murchison's[‖] Bamberger's[¶] and Fritz'[**] cases, nervous symptoms lasted for 5 days: in Coats'[††] and Merbach's[‡‡] cases for 8 or 9 days. In Dr. Wadham's case the man began to be confused in mind on Oct. 20 and did not die till Nov. 2.*

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[*] Chaumel, *Gaz. d. Hop.* 1863, p. 309.

[†] Waldeyer, *Arch. f. path. Anat.* 1868, Bd. xliii. p. 533.

[‡] Stehberger, *Arch. d. Heilk.* 1866. Jhg. vii. p. 282.

[§] Suringar (Canstatt's *Jahresb. f.* 1855, Bd. iii. p. 304) says in his case all the symptoms of acute yellow atrophy were present, but does not go further into detail, and no nervous symptoms are expressly named. So Klob (*Zeitschrift d. kk. Gesell. d. AA. zu Wien*, 1858, p. 736.) And Biermer (Virchow and Hirsch's *Jahresb. f.* 1869, Bd. ii. p. 5) speaks of a case of catarrhal jaundice lasting for some weeks, in which a hæmorrhagic diathesis developed itself with fever and large spleen, and death with dyspnœa and insensibility, but no examination with the microscope seems to have been made.

[‖] Murchison, *Clinical Lectures on Diseases of the Liver*, London, 1868, p. 236.

[¶] Bamberger, *Verhandlungen der phys. med. Gesellschaft in Würzburg*, 1858 Bd. viii. p. 268.

[**] Fritz, *Gaz. d. Hôp.* 1863, p. 81.

[††] Coats, *Brit. Med. Journal*, 1875, Vol. i. p. 847.

[‡‡] Merbach, Schmidt's *Jahrbb.* 1863, Bd. cxix. p. 38.

In Spengler's case, the woman began to be delirious on July 29, and nervous symptoms continued till death on Aug. 13.† As a rule the nervous symptoms go on from bad to worse, but very rarely indeed do they intermit as in one of Homans' cases.‡ But in the large majority of cases the nervous symptoms do not last more than 48 hours after they first set in.

The cause of the nervous symptoms is still very obscure, no theory of their nature being yet generally accepted. A theory which still largely prevails attributes the phænomena to the action of the bile circulating in the blood. Budd rejects this theory because he thinks that "there is abundant evidence to show that the mere retention of bile in its natural state produces no such effects."§ He then says that two other theories remain: the first is that the head symptoms are caused by the direct action of the poison which caused the jaundice. He rejects this on account of the sudden appearance of the symptoms, and inclines to the second theory; that the nervous symptoms are caused by decomposition in the liver, a poison being generated in this organ, which is the real cause of the malignant symptoms. These notions could only prevail so long as the liver be looked on as the only organ involved: with the knowledge that all the glands were affected different theories began to prevail.

Thus Rokitansky, finding that the kidneys suffered as much as the liver, suspected that the nervous phænomena were in great part due to uræmia;|| an

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* Wadham, *Lancet*, 1872, Vol. i. p. 288.

† Spengler, *Arch. f. path. Anat.* 1854, Bd. vi. p. 129.

‡ Homans, *American Journal of Med. Sciences*, 1868, Vol. lvi. p. 60.

§ Budd, *On Diseases of the Liver*, London, 1857, Third edition, p. 269.

|| Rokitansky, *Zeitschrift d. kk. Gesellschaft d. Aerzte zu Wien*, 1859, p. 500.

opinion to which Frerichs seems to point.* Like Budd he rejects all notion of cholæmia and speaks of the absence of urea in the urine and its accumulation in the blood. Bamberger agrees with Frerichs in not looking upon the nervous symptoms as due to cholæmia, nor does he think them caused by any change in the brain; he thinks it still very questionable if they be due to the general state.†

Leyden clearly thinks that much of the phænomena of *icterus gravis* may be explained by the poisonous action of the bile acids. He says that animals, into whose blood bile acids have been thrown, show nervous symptoms identical with those of acute yellow atrophy, such as coma and occasionally convulsions, and he would therefore believe that the symptoms in man are due to the presence of bile acids absorbed from the liver.‡ It may be remarked in reference to this theory that, if the nervous symptoms be due to the presence of the bile acids in the blood, it is strange that they do not show their physiological action on the heart; for the pulse which has been normal or slow up to the entrance of the nervous symptoms immediately becomes more rapid when they appear. If the bile acids produce their physiological action upon the brain, why not upon the heart?

Traube thinks that it is impossible that uræmia is the cause of these nervous symptoms: because i. there is no albumen in the urine and no disease of the kidney; ii. the nervous symptoms are not those of uræmia; in uræmia there are *prodroma*, bad headache, vomiting, decrease in number of the beats of the pulse, sometimes sudden blindness without recognisable disorder of the retina; then the convulsions come on and can in no way be distinguished from those of epilepsy: last, deep coma, and increase of the tension of the aortic system. It is rare in uræmia to see only coma. Now in acute yellow atrophy, there are never seen sudden blindness, convulsive attacks like those of epilepsy, increase of the tension of the arteries, nor after death that peculiar swelling of the brain which Traube looks upon as pathognomonic of uræmia.*

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* Frerichs, *op. cit.* Bd. i. pp. 240 and 242.

† Bamberger, *Khten. d. chyl. Syst.* Erlangen, 1864, p. 539.

‡ Leyden, *Beiträge zur Pathologie des Icterus*, Berlin, 1866, p. 176.

This is an instance of the extraordinary statements to which physicians of known reputation sometimes commit themselves. Nearly every one of Traube's statements may be denied. In the first place it will be shown, when the morbid anatomy of this disease is spoken of, that so far from it being a fact that in a great part of these cases no disease of the kidney can be made out, the contrary prevails, that, in fact, in the greater part of these cases very extensive and destructive disease of this organ is present, a disorder in every way akin to Bright's disease. Neither does it seem to me that the absence, in some cases, of albumen in the urine negatives the idea of uræmia, when such extensive kidney change is present. In the second place, vomiting and headache, are not uncommon symptoms as *prodroma* of the nervous attacks in acute yellow atrophy. Vomiting has been thought by Liebermeister to be one of the most common symptoms known.† Then cases can be brought forward which disprove the assertion that blindness is never known, and as to the statement that epileptiform attacks are never seen in acute yellow atrophy, one can only wonder at its audacity. Upon the tension in the arterial system no observations seem, unfortunately, to have been made in acute yellow atrophy.

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* Traube, *Berlin. klin. Wochenschrift*, 1867, p. 488. Reprinted in *Ges. Beit.* Berlin, 1871, Bd. ii. p. 820.

† Liebermeister, *Beiträge zur path. Anat. u. Klinik d. Leberkrankheiten*, Tübingen. 1864, p. 259.

Traube does not, however, think the symptoms due to cholæmia, for as much as they in no way resemble the symptoms which follow the injection of bile acids into the blood. He avails himself of H. Weber's theory of the delirium in pneumonia, and which may be called the inanition theory, that the brain is ill-supplied with poor blood by a weak heart. The same happens in jaundice. The bile acids injure the blood corpuscles, and the absence of bile in the intestines tends to lower the powers of nutrition and absorption; the nutrition of the brain is thus rapidly brought to a *minimum*.

Dr. Austin Flint, the younger, has laboured to prove that the nervous symptoms are all due to the presence of cholestearin in the blood. Cholestearin, if not allowed to pass out of the system by the bile, accumulates in the blood and causes a blood poisoning, which Dr. Flint calls cholestearæmia.[*] Koloman Müller has published some experiments in support of Dr. Flint's views.[†] But several observers seem to have conclusively shown that cholestearin is quite a harmless substance; and that the severe symptoms which followed its injection are due to the imperfect solution of the cholestearin, which therefore sets up abundant capillary embolisms; and the grave symptoms, thought to be the result of the injection of the cholestearin, are simply due to the numerous solid bodies thus brought into the circulation.[‡]

Hitherto only those theories which refer the symptoms to some general disorder have been spoken of. Early, however, in the history of the disease, Horaczek drew attention to changes in the brain itself. It is, says he, more often anæmic than full of blood, constantly infiltrated with serum, softened as in hydrocephalus, and sometimes reduced to a pulp.[*] Buhl mentions an acute atrophy or acute œdema in this disorder.[†]

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[*] Austin Flint, Junior, *American Journal of the Medical Sciences*, 1862, Vol. xliv. p. 305. For results see p. 362. This article has also been published separately in French at Paris, 1868.

[†] Koloman Müller, *Arch. f. exp. Path.* 1873, Bd. i. p. 213.

[‡] Feltz and Ritter, *Journal de l'Anatomie et de la Physiologie*, 1875, t. xi. p. 165 and V. von Krusenstern, *Arch. f. path. Anat.* 1875, Bd. lxv. p. 410. See also p. 222 of this work.

Monneret suggested that the nervous symptoms were due to hæmorrhage into the meninges; first causing convulsions, clonic or tonic, and then coma.[‡] These remarks, however, seemed altogether forgotten. No one in recent times has thought the brain worthy of much attention, for all seem to work upon the nervous symptoms as part of a general state. It is possible, however, that the brain, in all these delirious states, may prove to be the chief organ disordered. It will be at once allowed that no appearances of disease can be made out by the naked eye; but in the one case[§] in which the blood vessels of the brain have been examined with the microscope, marked changes were found. The walls showed a cloudy swelling precisely akin to that which goes on in the rest of the vessels of the body, changes which Wunderlich has shown to take place.[‖] If extensive changes in the cerebral vessels and circulation take place, it is no wonder that nervous phænomena should be seen; and to changes such as Steiner and Wunderlich have described, I feel inclined to attribute the nervous symptoms of acute yellow atrophy.

ii. Of the graver symptoms, next to the nervous phænomena, hæmorrhages of all kinds, from the mucous membranes, into the skin and serous membranes, and even from wounds, are most commonly seen. Ozanam noticed the hæmorrhagic diathesis,[*] a few years later Buhl,[†] Budd,[‡] and Monneret,[§] pointed out the occurrence of numerous hæmorrhages in acute yellow atrophy. Liebermeister showed how common the hæmorrhagic diathesis was. Out of 115 cases of fatal acute yellow atrophy, hæmorrhages were spoken of in 82.[‖] Out of my own hundred cases I find the proportion still higher; in only 20 cases is there no mention of hæmorrhage. In the remaining 80 there are bleedings, sometimes slight, sometimes profuse, and in many they were only discovered after death. I believe myself that the proportion of 80 in 100 is still too low; and that if all the cases had been thoroughly reported, the ratio would have been still higher.

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[*] Horaczek, *Die gallige Dyscrasie*, Wien, 1843, p. 8.

[†] Buhl, *Zeitschrift f. rat. Med.* 1857, Bd. viii. N. F. p. 43.

[‡] Monneret, *De l'ictère hémorrhagique essent.* Paris, 1859, p. 19.

[§] Steiner, *Jahrbuch f. Kinderheilk.* 1871, Bd. iv. N. F. p. 430.

[‖] Wunderlich, *Arch. d. Heilk.* 1863, Bd. iv. p. 149.

The most common of these bleedings is the hæmorrhage into the stomach, shown by black vomit during life, or after death by discovering changed blood in the stomach. Another common place for hæmorrhage is into the intestine, and the patient passes very dark-coloured stools, melæna. Next to hæmorrhages into the alimentary canals, epistaxis is most often seen. The hæmorrhages which follow are rarer. Ecchymoses and petechiæ in the skin, bleedings from wounds such as leech bites,[¶] or from the gums, and blood in the urine.[**] In women who have aborted there is sometimes flooding, which may kill as in Stehberger's second case.* Hæmorrhages from the genitals may be seen in women who are not pregnant.† The patient sometimes dies bringing up bloody foam from the chest or black vomit from the stomach. The hæmorrhages seen after death will be described in the chapter on morbid anatomy. These are sometimes the most important, as there may be no signs whatever during life of hæmorrhage under the pleura, pericardium or omentum.

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[*] Ozanam, *op. cit.* p. 20.

[†] Buhl, *Zeitschrift f. rat. Med.* 1854, Bd. iv. N. F. p. 354.

[‡] Budd, *On Diseases of the Liver*, Lond. 1857, p. 259. Not in first ed. of 1845.

[§] Monneret, *de l'ictère hémorrhagique essentiel*, 1859, extrait du *Journal du Progrès.*

[‖] Liebermeister, *Beiträge zur path. Anat. u. Klinik d. Leberkrankheiten*, Tübingen, 1864, p. 258.

[¶] Porter, *Am. Journal of the Med. Sciences*, 1871, Vol. lxi. p. 150. From ulcers on the prepuce, Krafft-Ebing, Virchow and Hirsch's *Jahresb. f.* 1871, Bd. ii. p. 161.

[**] Buhl, *op. cit.* p. 352. Monneret, *op. cit.* p. 18. Pleischl und Folwarczny, *Zeitschrift d. k.k. Gesellschaft d. AA. zu Wien*, 1858, p. 623. Schultzen and Riess *Annalen d. Charité-Krankenhauses*, 1869, Bd. xv. pp. 65, 80 and 85.

The hæmorrhages have no rule for making their appearances. They may appear before the nervous symptoms,‡ with them, or not until the moment of death, and they may only be discovered after death. In those rare cases such as Buhl's§ in which nervous symptoms are not marked, the hæmorrhages are an important aid towards forming a grave prognosis.

It is altogether a mistake to attempt to establish a hæmorrhagic jaundice as a separate species, as Monneret has done.‖ Hæmorrhages may be shown to be an almost constant accompaniment of severe jaundice, so that they cannot be looked upon as creating a distinct kind, any more than the delirium or high temperature can be thought to give a right to speak of *icterus gravis nervosus* or *icterus gravis febrilis.*

The cause of this hæmorrhagic diathesis has not been much discussed. Monneret, notwithstanding the great prominence which he gives to it, does not seem to have suggested any theory of its nature or its cause.¶ Budd attributed the hæmorrhages to the state of the blood.‡

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* Stehberger, *Arch. f. Heilkunde*, 1866, Jahrg. vii. p. 282.

† Christy Wilson, *Edinb. Med. Journal*, 1868, Vol. xiii. p. 736.

‡ Bergeron, *Union méd.* 1862, t. xiv. p. 567.

§ Buhl, *Zeitschrift f. rat. Med.* 1854, Bd. iv. N. F. p. 352.

‖ Monneret, *op. cit.*

¶ Frerichs says that Monneret thinks it due to lack of fibrin in the blood. (Bd. i. p. 242.)

‡ Budd, *op. cit.* p. 267.

Buhl, to the weakened action of the heart.[*] Frerichs, to some change in the blood and its adhesion to the vessels.[§] Traube found that whenever he injected bile acids into the carotid towards the brain, an ecchymosis appeared on the conjunctiva,[‡] and Leyden also noticed the same appearance in animals whose bile duct he had tied,[§] so that, on these facts, it would not seem unlikely that the hæmorrhages were due to the circulation of the bile acids in the blood. Pagès thinks the hæmorrhages are caused by capillary emboli of fat and crystals of cholestearin.[‖]

Hæmorrhages, in my opinion, are more often caused by a change in the walls of vessels than by changes in the blood; and it seems that Wunderlich has probably hit upon the right path of explanation when he shortly points out that the fatty degeneration of the walls of the vessels may have hæmorrhage as a consequence.[¶] At this same view Picot has arrived,[§] apparently quite independently of Wunderlich.

It has already been noted that hæmorrhages into the alimentary tract are more common than into other parts. Budd believes this to be due to a special congestion of the parts,[*] but how this arises is not at all clear, unless indeed a formation of new connective-tissue or cirrhosis be allowed in all cases of acute yellow atrophy.

iii. So long as the jaundice remains uncomplicated, the temperature and pulse remain natural, or even below the natural height and number of beats; in some cases the temperature is but 96° (35° ·5) and the pulse

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[*] Buhl, *op. cit.* p. 355.

[†] Frerichs, *op. cit.* Bd. i. p. 242.

[‡] Traube, *Berlin. klin. Wochenschrift*, 1864, p. 147 and *Ges. Beiträge*, Berlin, 1871, Bd. i. p. 366.

[§] Leyden, *Beiträge zur Pathologie des Icterus*, Berlin, 1866, pp. 87 and 88.

[‖] Pagès, *de la cholestèrine*, Thèse de Strasbourg, 1869, p. 31.

[¶] Wunderlich, *Arch. d. Heilkunde*, 1860, Jahrg. i. p. 232.

[**] Picot, *Journal de l'Anatomie*, 1872, p. 262.

[††] Budd, *op. cit.* p. 267.

60. But as soon as the nervous symptoms arise a change may be looked for. A rise in the temperature and in the pulse should be watched against in every case that is seen, although the rise in temperature is not constant and some cases are certainly seen without any pyrexia.

It did not escape Horaczek's notice that the temperature and pulse became raised; he speaks of the high temperature, however, as a symptom peculiar to the agony.* Frerichs says the pulse begins to rise when the nervous symptoms set in, and from 50 to 60 passes to 90 and 100; at the same time it shows fluctuations, rising from 100 to 120 or 130, to fall again to 80 or 90. With the deep coma, the pulse goes up to 140 or 150 beats while it becomes small and thread-like.†

Frerichs' statement is no doubt true of a great number of cases, but there are some which run their course without the pulse showing any remarkable variations from the natural number of beats, or it may even keep below the natural standard.‡ Neither does it always follow the fluctuations of the temperature; in Sotti's case, the pulse kept quite natural (below 100) when the evening temperature was over 106° F. (41·2° C.)§

It cannot be looked for that any accurate observations on the temperature of the body in acute yellow atrophy should have been made before the general introduction of the use of the thermometer into medical practice. Thus nearly all the cases in which the temperature has been recorded are within the last twenty years, and not more than thirty-one writers seem to have taken much interest in this point. The materials for forming a just opinion are small.

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* Horaczek, *Die gallige Dyscrasie*, Wien, 1843, p. 23.

† Frerichs, *op. cit.* Bd. i. p. 225. In one of Bamberger's cases the pulse went up to 172. (*Deutsche Klinik*, 1850, p. 98.)

‡ In a case of Budd's (*op. cit.* p. 256) the pulse, so far as can be gathered, seems to have never been more than 60 throughout the nervous symptoms.

§ Sotti, *Gazetta Medica Italiana-Provincie Venete*, 1872, Anno xv. N. 18°.

The temperature of the body shows much less regularity in its course than the pulse; there are nineteen cases on record in which the temperature has been high, that is over 100° F. or 37·5° C. While in fifteen others the temperature has never been noted over this point. The temperature does not seem to be influenced by the age, nor sex of the patient; nor in women by the fact of pregnancy. Of these nineteen cases there are eight in which the temperature varied from 100·4 F. (38° C) to 102·2 F. (39° C.) without going higher. In the remainder it touched 104° F. (40° C.) or even higher. These higher temperatures seem to be the forerunners of death for all, but the temperature did not begin to rise till a few hours before death. The highest temperature was taken in Dr. Sieveking's case, in which the thermometer in the axilla rose to 106·5° F. (41·4° C.) seven hours before death.[*] Usually the thermometer stands at its highest just before death, but there are exceptions to this, as in Rosenstein's case.[†]

In the remainder of the cases the temperature was low, even below normal, whenever it was taken; but in some of these it seems only to have been taken once, and in others no observations were made at the approach of death.

It is very rare for the temperature to rise before the nervous symptoms set in. Burkart has indeed described a case of this sort in which the temperature rose in the midst of a simple jaundice to 39·2°

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[*] Sieveking, *Lancet*, 1872, Vol. ii. p. 224. In Dupré's case the temperature an hour before death was 107·6 F. (42° C.) but the microscope was not used after death. (*Ueber Icterus gravis bei Schwangern*, Strassburg, 1873, p. 29.) There are three other cases in which the temperature was high at the moment of death, but there is no record of use of the microscope after death. In Chamberlain's case which I have not reckoned, the temperature was only 96·5° F. the day before death, but "catalytic heat developed just before death." (*New York Med. Record*, 1871, Vol. vi. p. 266.)

[†] Rosenstein, *Berlin. klin. Wochenschrift*, 1868, p. 161. Cf. Christy Wilson, *Edinb. Med. Journal*, 1868, Vol. xiii. p. 737.

C. and at the same time a macular exanthem appeared on the chest and belly very like the measles, so that it was thought that the patient was about to have an attack of the small-pox. The next day, the rash, however, began to disappear while the fever increased, and at night there was delirium, and the patient died of acute yellow atrophy on the fourth day after the onset of the fever.[*] Sotti also noted a great rise of temperature (40·5° C. 105° F.) preceded by rigors, eight days before death, while no marked nervous symptoms were present until the next day when a severe headache declared itself; coma only set in two days before death and the temperature at the onset of the coma was lowered.[*] (38·4° C. 101·9° F.)

Bamberger gives a very different account from the foregoing. He says that with the appearance of nervous symptoms, or shortly before that, the pulse and temperature go up; but that, at the height of the nervous symptoms, especially when coma begins, the pulse falls to 60 or lower, and the skin becomes cool and wrinkled. Still there are cases where a rapid pulse may be seen during coma. Towards the end of life, the pulse rises, and abundant perspiration comes on, although at the very end the pulse is often not to be felt.[*]

More in accordance with the opinions that I have formed is Traube's statement that, however severe the nervous symptoms or convulsions may have been, yet the temperature remains normal, unless the last few hours before death be excluded.[‡]

No observations seem yet to have been made on the rise of temperature after death; a point for investigation which may be recommended to coming observers.

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[*] Burkart, *Ueber acute gelbe Leberatrophie*, Inaug. Diss. Stuttgart, 1872, p. 4.

[†] Sotti, *loc. cit.*

[‡] Bamberger, *op. cit.* p. 533.

[§] Traube, *Berlin. klin. Wochenschrift*, 1867, p. 499.

iv. From the great decrease in the size of the liver found after death, the attention of physicians was soon called to the state of this organ during life, and the increase or decrease of the amount of percussion dulness, and the possibility of feeling the liver. Horaczek speaks of the information given by percussion and palpation,* though Budd does not seem to have used percussion.† Frerichs laid great weight upon it, making the gradual decrease of the percussion dulness one of the diagnostic notes of acute yellow atrophy.‡ Since that time percussion seems to have been universally employed in this disorder.

Liebermeister has shown that in the first stage of acute yellow atrophy, the liver is really larger than natural, and that it is only at the very end of the disorder that the shrinking and smallness of the organ are observed.§ So that at first the liver may be expected to be found of normal size or larger than natural. Quickly, however, the liver decreases in size, and this may, in favourable cases, be revealed to percussion. The decrease may be so great that no liver dulness whatever may be detected. Still the liver may remain of natural size to percussion throughout the whole of the disease, and this seems to be very commonly the case in children. On the other hand the liver dulness may be greatly decreased, and decrease from day to day in what might be thought a characteristic manner, and yet, after death, the liver may be found of natural size and weight. A very instructive instance of this is published by Burkart. The liver on Oct. 27 was found to stretch 3 fingers' breadth below the ribs: on Nov. 4, nervous symptoms set in and the liver dulness, beginning two fingers' breadth below the nipple, was found to be only three fingers' broad: on the 6th the dulness was further diminished; the next day the dulness is said to be reduced to a *minimum* and the patient died soon after this observation was made. Yet the liver was found to weigh 1740 grammes, about 58 ounces, which is high for a girl of 20 years old.[*] This deceptive decrease of the percussion dulness seems best explained by an increase of the air contained in the large intestine. It is not confined to cases of acute atrophy, but may be seen in simple jaundice and give rise to great and unnecessary alarm.[†]

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* Horaczek, *Die gallige Dyscrasie*, Wien, 1843, p. 20.

† Budd, *op. cit.* p. 288.

‡ Frerichs, *op. cit.* Bd. i. p. 246.

§ Liebermeister, *op. cit.* p. 230.

Riess mentions a fact which serves to show the untrustworthiness of percussion in these cases. The day before the death of a patient with acute yellow atrophy, he was examining the liver; and while percussion was being employed, the lower limit of the liver dulness suddenly went up at least an inch, plainly due, says Riess, to the peristaltic movement of the bowels pushing a coil up and causing the tympanitic sound.[‡]

If the liver decrease in size, another organ, a close neighbour, increases in size. The spleen is found, in nearly all cases, enlarged.[§] But this enlargement, although it should always be looked for, cannot often be detected during life. Frerichs says that if it cannot be found out, it is always due to old adhesions to the diaphragm or thickening of the capsule.* I do not think that this is really the cause; but that the spleen, although enlarged, is not sufficiently so to be readily felt or percussed: the cause of the small increase may be, as Frerichs suggests, abundant hæmorrhage from the stomach and intestines emptying the portal venous system. Liebermeister rejects this and thinks that in all cases the increase of the spleen depends on the decrease of the liver in size.† In some few cases the spleen remains normal in size or even smaller than natural.

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[*] Albert Burkart, *Ueber acute gelbe Leberatrophie*, Diss. Inaug. Stuttgart, 1872, pp. 4 and 6. Cf. Coats (*Brit. Med. Journal*, 1875, Vol. i. p. 847.) The hepatic dulness in line of axilla was only 2½ inches, yet after death the liver weighed 44½ oz.

[†] A boy, 10 years of age, was admitted into St. Bartholomew's Hospital for simple jaundice; the liver could be felt two fingers' breadth below the ribs. After a fortnight's stay in the Hospital he became dull and apathetic, almost comatose, with dilated pupils: at the same time the liver dulness was found to be almost gone. On smart purging, the head symptoms went off, and the liver came back to the same size that it was on admission. It cannot be thought in this case that the liver first became small and again enlarged.

[‡] Riess, *Annalen d. Charité-Krankenhauses*, 1864, Bd. xii. Heft ii. p. 127.

[§] Horaczek, *op. cit.* p. 21.

v. The symptoms which now remain to be discussed are those which are less prominent, and so do not attract much attention from the cursory observer. Amongst the most constant of these are vomiting and pain in the epigastrium. It has been remarked that the symptoms in a large number of cases begin with those of a gastric catarrh; but although nausea is common enough, vomiting is not so marked at this stage of the disease. Liebermeister seems inclined to believe that vomiting is a tolerably constant phænomenon, for he says that out of 124 cases vomiting was noted in 76.‡ In my own 100 cases, vomiting at one time or other of the disease was noted in 55 cases. I have been liberal in admitting cases, for if there were evidence that the patient vomited but once at any stage of the disease, I have placed the case among the 55. In the remaining 45 there is no mention of vomiting, and this may be due to deficiency in the clinical reports, but there are many in which full reports are given and yet nothing is said about vomiting. In 34 only, can vomiting be said to be marked. In the others the vomiting may be seen only in the *prodroma* of the disease, during the jaundice, or at the very end, and lasting for a very short time.

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* Frerichs, *op. cit.* Bd. i. p. 228.

† Liebermeister, *op. cit.* p. 231.

‡ Liebermeister, *op. cit.* p. 259.

The vomited matters may at the beginning of the disease be pale in colour, merely the ingesta; sometimes they are said to be bilious. Towards the end of the disease they are commonly black, from the presence of altered blood, and this is a very grave symptom, that ushers in the fatal ending. Sometimes there is no vomiting whatever, till the black vomit appear, and in some cases this is only seen an hour or two before death, or indeed almost in the moment of death.

Pain, or rather tenderness, of the epigastrium and hypochondria is a very common symptom. Frerichs says that pain is present in three-fourths of the cases;* but on the other hand Liebermeister says that Bamberger met with this symptom in one only out of six cases.† Out of my own hundred I found distinct tenderness spoken of only 35 times. In the rest it is not spoken of or else distinctly denied, and of this last there are many cases. The pain is commonly not complained of, as the patient is comatose, and it is only by pressing on the part that an expression of suffering is given to the face. Sometimes, however, the pain and tenderness come on before the coma, as in the second of Pleischl and Folwarczny's cases, where the pain in the belly and vomiting of blood came on six days before the jaundice and nervous symptoms, and eight days before death.‡ In some cases there can be no doubt that Bamberger is right in attributing the tenderness to a general hyperæsthesia and not to a local tenderness of the liver or stomach,§ but in others it would seem, together with the vomiting, to be due to the active changes which take place in the stomach in the degeneration of the peptic glands.

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* Frerichs, *op. cit.* Bd. i. p. 227.

† Liebermeister, *op. cit.* p. 258.

‡ Pleischl und Folwarczny, *Zeitschrift d. kk. Gesellschaft d. AA. zu Wien*, 1858, p. 608.

§ Bamberger, *op. cit.* p. 533.

Diarrhœa and costiveness seem to prevail in almost equal degree; in the former case the stools with the urine are passed under the patient. They are usually free from bile, like porridge in consistence, and are often black from the admixture of blood at the end of the disease. If the costiveness prevail, then no stools are seen unless purgatives such as calomel or croton oil be given.

The state of the tongue is by no means constant. In some it is clean and dry; in others, furred; in others, red, raw, and glazed; and again in others brown and dry like that of a typhus patient.* In many cases sordes are spoken of on the lips and teeth.

Frerichs compares the breathing at the end of the disease to that of an animal, both of whose *vagi* have been cut. The breathing becomes sighing or stertorous; a short groaning inspiration is followed by a rapid expiration, and then a long pause.† These phænomena are only seen late in the disease; at first the breathing is natural.

In one of Traube's cases there was seen in the midst of the nervous symptoms well-marked Stokes' breathing.‡ This may be considered side by side with the fact that the injection of the bile acids into the carotid is followed by a deep inspiration, after which the chest walls are for some time held expanded.

The older cases sometimes showed symptoms which in these later times have not been noticed. For instance, Ozanam speaks of roseola and prurigo and miliary eruptions, of which the most common is certainly roseola. This roseola rarely appears at first. Usually it is seen from the seventh to the fourteenth day. Ozanam thinks the roseola peculiar to *icterus gravis*, and that it might even serve as a means of diagnosis between this disease and typhoid fever accompanied by jaundice.*

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* Dr. Murchison (*op. cit.* p. 229) says that this is an "almost invariable" appearance. I fear that I cannot, in the face of many cases in which the contrary is asserted, allow this statement to be even approximatively true.

† Frerichs, *op. cit.* Bd. i. p. 226.

‡ Traube, *Berlin. klin. Wochenschrift*, 1867, p. 489.

Lebert speaks of an eruption on the skin seen in a sixth of the cases, appearing on the fourth to the eighth day after the jaundice; two forms being seen, one red, disappearing on pressure, like the typhoid roseola; the other more petechial in character yet bigger than ordinary vibices. The limbs, not the trunk, are the favourite seat of this eruption.† Frerichs does not seem to mention this eruption and Bamberger says he has never seen it.‡ Not many writers of late have spoken of this peculiar eruption; even if the cases complicated with syphilis be set aside,§ but few seem to record an eruption at all like to that of typhoid fever.

Burkart, before the jaundice appeared, saw an eruption like that of the measles, that with the other severe symptoms it was thought that an attack of the small-pox was at hand.‖ In Dr. Hilton Fagge's case there was thought to be a red rash on the skin, but this was set down to a supposed belladonna poisoning.¶ In Chaumel's doubtful case there was an eruption of red spots thought to be erythema.** And in London's case, in which no examination of the liver after death was made with the microscope, there was a roseola over the breast at the time of admission.[*] In Leichtenstern's case of recovery there was an eruption over the chest, which made its appearance when the nervous symptoms had passed off, and the patient was beginning to recover.[†] In another case of recovery, recorded by Brouardel, there was a papular erythema over the belly and upper part of the thighs on the day of admission; this eruption had disappeared on the second day, about the time that the graver symptoms appeared.[‡]

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* Ozanam, *op. cit.* p. 37.

† Lebert, *Arch. f. path. Anat.* 1854 d. vii. p. 367.

‡ Bamberger, *op. cit.* p. 534.

§ Riess, *Annalen d. Charité-Krankenhauses*, 1865, Bd. xii. Heft ii. p. 141. Cf. Goodridge, *Brit. Med. Journal*, 1871, Vol. i. p. 609.

‖ Albert Burkart, *Ueber acute gelbe Leberatrophie*, Diss. Inaug. Stuttgart, 1872, p. 4. Cf. Rayer, *Gaz. d. Hôp.* 1845, p. 369.

¶ Hilton Fagge, *Trans. of the Path. Soc. of Lond.* 1869, Vol. xx. p. 212.

** Chaumel, *Gaz. d. Hôp.* 1863, p. 309.

Danielssen has described a case of *icterus gravis* after scarlet fever in a girl of twenty. The macular eruption was thought to be cured when death took place on the sixth day after the eruption. After death a fatty change, rapidly developed, was found in the liver, spleen, kidneys and heart, with considerable ecchymoses of the lungs and kidneys.[§]

In Dr. Moxon's case pruritus and eczema followed the use of a nitro-hydrochloric acid bath.[||] This can scarcely be confounded with the eruption spoken of by Lebert; nor can the erysipelas which Dr. Handfield Jones[¶] and others have described be thought to be a part of the disease.

A symptom noted in some of the earlier cases was a parotitis, and this, like the roseola, is but rarely mentioned in the more modern reports. It was noted in Chaumel's case and these went on to suppuration.[**] Lebert says that he was only able to find one of these cases, that it ended without suppuration and in recovery.[*] Quinquaud's case, of which doubt may be entertained as to the diagnosis, went on to suppuration, but ended in recovery.[†]

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[*] London, *Wien. med. Wochenschrift*, 1865, p. 697.

[†] Leichtenstern, *Zeitschrift f. rat. Med.* 1869, iii. Reihe, Bd. xxxvi. p. 241.

[‡] Brouardel, *Arch. d. Physiologie*, 1876, p. 409.

[§] Danielssen, *Bericht ueber die Wirksamkeit des Lungegaards-Spitals im Triennium* 1865-67. Reported in Virchow and Hirsch's *Jahresb. f.* 1868, Bd. ii. p. 255.

[||] Moxon, *Trans. of the Path. Soc. of Lond*, 1872, Vol. xxiii. p. 138.

[¶] Handfield Jones, *Lond. Med. Gaz.* 1847, N.S. Vol. v. p. 1145.

[**] Chaumel, *loc. cit.* Cf. Liégey, *Union méd.* 1863, t. xvii. p. 104. Bouillaud, *Gaz. d. Hôp.* 1862, p. 109. In this case the parotid swelling disappeared before the jaundice.

In some other of these older cases, an injection of the conjunctiva was seen. Lewis Mackenzie noticed the same in his undoubted case. There was a redness of the conjunctiva like that commonly seen in catarrhal ophthalmia.[‡]

The interest which such symptoms as a roseolous eruption, a parotitis, and injection of the conjunctivæ arouse is due solely to the fact that similar appearances are seen in yellow fever. As will be hereafter shown, yellow fever has a great affinity to acute yellow atrophy seen from a morbid anatomy point of view.

The Urine. The urine in acute yellow atrophy has of late years very properly received a great deal of attention, though it can scarcely be said to have been studied until the time of Frerichs. This observer made two important statements: i. that leucin and tyrosin appeared in the urine; and ii. that the urea and earthy phosphates disappeared from it.[§] From that time few observers have failed in some degree to examine the urine.

The reaction seems to be always acid, except in the case of Steiner's,[‖] in which it was neutral and Schultzen and Riess', in which it was alkaline.[¶] In colour it varies with the intensity of the jaundice, though it seems but rarely to be very dark. The specific gravity ranges from 1015 to 1030; rarely higher or lower than this.[**]

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[*] Lebert, *loc. cit.* [†] Quinquaud, *Les Affections du Foie*, Paris, 1879, p. 86.

[‡] Lewis Mackenzie, *Brit. Med. Journal*, 1874, Vol. ii. p. 107. Animals poisoned by phosphorus often show a muco-purulent conjunctivitis; not, however, seen in men poisoned by the same body.

[§] Frerichs, *op. cit.* Bd. i. p. 228.

[‖] Steiner, *Jahrbuch f. Kinderheilkunde*, 1871, Bd. iv. p. 428

[†] Schultzen and Riess, *Annalen d. Charité-Krankenhauses*, 1869, Bd. xv. p. 48.

[**] Schultzen and Riess (*op. cit.* p. 90) found in their four cases the specific gravity to vary between 1016 and 1030.

There are but few accurate observations on the amount of urine excreted in twenty-four hours. It appears to be almost natural in amount early in the disease; but accounts vary even as to this; and towards the close of the disorder is often very scanty, if not altogether suppressed, so that no urine comes away, even if the catheter be introduced into the bladder.[*] Of course in many acute diseases the urine becomes decreased towards the end, and it remains to be seen if this be a peculiarity of acute yellow atrophy.

In Dr. Grainger Stewart's case, Dr. Arthur Gamgee found the total solids only 2·194 in 100,[†] but in the third of Schultzen and Riess' cases 10 C.C. of the urine dried at 110° C. yielded ·6891 grm. that is much over 6 *per cent.* of total solids; after incineration there was ·0468 grm. residue.[‡] Frerichs in one of his cases found 4·9 *per cent.* of total solids and ·14 *per cent.* of ash.[§] In health the amount of total solids varies between 2 and 7 *per cent.* so that there does not seem, as far as forthcoming analyses go, to be any great decrease or increase in the amount of solids.

Frerichs' statement that the urine no longer contains urea has already been spoken of. Most contradictory observations on this head are recorded: some stating that the urea is increased; for example, Rosenstein found the urine in one of his cases to contain 2·25 *per cent.* of urea about 36 hours before death, and in that taken from the bladder about 12 hours before death to contain 3 *per cent.*[‖] In Matterstock's first case the amount of urine was 3000 C.C. in the 24 hours, specific gravity 1010 and the percentage of urea 1·5, that is about 45 grm. for the 24 hours. In the second case, the urine was 1300 C.C. in the twenty hours, and 1·55 *per cent.* of urea, that is, about 20·15 grm. In both these cases, however, the diagnosis was not put beyond a doubt by examination of the liver with the microscope.[*] In one of Dr. Wilks' cases, Dr. George Harley found the urea to be 3 *per cent.*[†]

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[*] Coats, *Brit. Med. Journal*, 1875, Vol. i. p. 847. Davidson, *Monatsschrift f. Geburtskunde*, 1867, Bd. xxx. p. 452.

[†] Grainger Stewart, *Edinb. Medical Journal*, 1866, Vol. xi. p. 327.

[‡] Schultzen and Riess, *op. cit.* p. 80.

[§] Frerichs, *op. cit.* Bd. i. p. 216.

[‖] Rosenstein, *Berlin. klin. Wochenschrift*, 1868, p. 161.

Huppert found that from the 16th to the 19th day of the disease, the urine was 1950 to 1870 C.C. in quantity, and the urea sank from 37·44 grm. on the 16th to 21·7 grm. on the 19th, the day on which the patient became sleepy. On the 22nd and 23rd days the urine was about 1350 C.C. and the urea about 33 grm. On the 24th day the patient died.[‡]

Rosenstein, Matterstock, Harley, and Huppert, do not give the method by which the urea was estimated, and Schultzen and Riess assume it in Rosenstein's case to have been by Liebig's method and to be thus altogether worthless. They have found a peptone-like body in the urine in acute yellow atrophy,[§] and which cannot therefore be got rid of by heat and acid, and the presence of which vitiates all estimations by the mercurial method. Scherer, however, found a good deal of urea when the urine was mixed with two parts of alcohol and one of æther, and the crystals of urea were recognised under the microscope.

In one of Sander's cases the urea was estimated by Liebig's process and the amount of urea in urine passed about 24 hours before death was certainly very low, 3·9 grm. in 500 C.C. In the 150 C.C. drawn off by the catheter in the last hours of life there were 2·5 grm. a decided increase, if the method of estimation be trusted.[*] Some authors, such as Dr. Murchison[†] and Baader and Winiwarter[‡] and Riess,[§] mention the presence of urea which they detected as nitrate or oxalate. Other writers content themselves with noting that the urea is decreased or present without giving particulars of the method employed. In this way Standhartner, after an analysis by Folwarczny, says the urea was in normal amount;[‖] the same is said by Petersen in Rehn's case.[¶] Dr. Ralfe found in a boy of 17 that the urea was but little diminished.[**]

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[*] Matterstock, *Wiener med. Wochenschrift*, 1876, pp. 882 and 883. Valenta (Virchow and Hirsch's *Jahresb. f.* 1869, Bd. ii. p. 149) found in the urine drawn from the bladder after death *ziemlich reichlicher Harnstoff;* but gives no numbers. Much the same expression is used by Scherer (*Verhandlungen d. phys.-med. Gesellschaft in Würtzburg*, 1858, Bd. viii. p. 282.)

[†] Wilks, *Trans. of the Path. Society of Lond.* 1862, Vol. xiii. p. 107.

[‡] Huppert, *Archiv der Heilkunde*, 1864, p. 254

[§] Schultzen and Riess, *op. cit.* p. 91.

In one of his cases Frerichs found no urea and in another but little.[††] Hoppe-Seyler, in the second of Sander's cases, found no urea whatever.[§] Schultzen and Riess, who have paid great attention to the urine in acute yellow atrophy, state that the urea is either entirely absent, or reduced to a *minimum*.[§§] Prof. Maisch found no urea in Dr. Wood's case.[†] Schmeisser says there was none in his case, though he remarks that some may have been present although nitric acid threw down no precipitate.[¶¶] In Lewitski and Brodowski's case of a boy of 15, only 8·48 grm. of urea were found in 1030 C.C. of urine obtained by the catheter, the day on which the nervous symptoms began, and the day before death. The method of estimation is not given.*

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[*] Sander, *Deutsche Klinik*, 1860, p. 33.

[†] Murchison, *op. cit.* p. 237.

[‡] Baader and Winiwater, *Wien. med. Wochenschrift*, 1870, p. 1404.

[§] Riess, *Annalen d. Charité-Krankenhauses*, 1864, Bd. xii. Heft ii. pp. 126 and 128.

[‖] Standhartner, *Zeitschrift d. kk. Gesellschaft d. AA. zu Wien*, 1858, p. 787.

[¶] Rehn, *Berlin. klin. Wochenschrift*, 1875, p. 650.

[**] Ralfe, reported by Leach, *Brit. Med. Journal*, 1878, Vol. ii. p. 877.

[††] Frerichs, *op. cit.* Bd. i. pp. 216 and 220.

[‡‡] Sander, *Deutsche Klinik*, 1862, p. 295.

[§§] Schultzen and Riess, *op. cit.* p. 91. It is a matter of some surprise to me, however, that in giving the details of their four cases, no mention is made of the urea when the analysis of the urine is spoken of.

[‖‖] H. C. Wood, *American Journal of the Med. Sciences*, 1867, Vol. liii. p. 422.

[¶¶] Schmeisser, Schmidt's *Jahrbb.* 1861, Bd. cix. p. 149.

In a case of Brouardel's, not one exactly typical of the course and symptoms of acute yellow atrophy, there was a great fall in the amount of urea, at the same time as the appearance of a persistent epistaxis, increase of the jaundiced tint, the state called the typhoid, and a temperature about 39·5° C. or 103° F. With an improvement in the general state, the urea also rose, but with many fluctuations.†

In observations to be made hereafter on the amount of urea, it will be impossible to use either Liebig's or Rüssell and West's method. Liebig's plan may be put aside altogether. Russell and West's method will give very interesting results as to the total amount of nitrogen, but if the nitrogenous bodies be present in large amount, a serious error will arise in the estimation of the urea. The other method which remains is that of Heintz and Ragsky.

Uric acid crystals seem to have spontaneously separated from the urine in Frerichs',‡ one of Homans',§ and in Steiner's,‖ cases. In one of Dr. Wilks' cases, Dr. George Harley found the uric acid to be ·375 in 1000.¶ In Riess' case urate of ammonia was found;** and uric acid was found in Dr. Grainger Stewart's, Dr. H. C. Wood's, Bamberger's, Rehn's, and Schultzen and Riess' cases. These last two observers say it is found in but small amount. Folwarczny in Standhartner's case found the uric acid increased.†† No uric acid could be found in Schmeisser's case.§§

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* Lewitski and Brodowski, *Arch. f. path. Anat.* 1877, Bd. lxx. p. 423.

† Brouardel, *Arch. d. Physiologie*, 1876, p. 409.

‡ Frerichs, *loc. cit.*

§ Homans, *Amer. Journal of the Med. Sciences*, 1868, Vol. lvi. p. 60.

‖ Steiner, *Jahrb. f. Kinderheilk.* 1871, Bd. iv. p. 428.

¶ Wilks, *loc. cit.*

** Riess, *Annalen d. Charité-Krankenhauses*, 1864, Bd. xii. Heft. ii. p. 126.

†† Standhartner, *loc. cit.*

§§ Schmeisser, *loc. cit.*

Next the inorganic salts are of some interest on account of the varying statements which have been made about them. Homans, for example, found the sulphates, phosphates, and chlorides, normal.[*] The same was found in Standhartner's case. Wunderlich,[†] Valenta,[‡] and Braun[§] found the chlorides decreased. Pleischl and Folwarczny found in their second case that the chlorides were entirely absent, the earthy phosphates decreased, the alkaline phosphates increased, no bone earth: in the third there was but little chloride but much alkaline phosphate.[‖] In Dr. H. C. Wood's case, there were present sulphates, a small quantity of phosphates, but there was a total absence of chlorides. In Dr. Grainger Stewart's case the chlorides and earthy phosphates were entirely absent, and only the faintest trace of phosphates was found. The only salts present were the alkaline phosphates. The earthy phosphates were entirely absent from the ash of one of Frerichs' cases. In Huppert's case, there were about 7 grammes of chloride of sodium passed daily until the nervous symptoms set in; after that they fell to 3 or even less than 3 grammes.[¶]

There are a large number of reports upon the presence or absence of albumen, the greater number asserting that the urine is free from albumen, while those which have been more carefully drawn up say that albumen is present although in very small quantity; such as a mere cloudiness after the adding of nitric acid to the boiling urine. In Oppolzer's case the urine is stated to have been highly albuminous.[**]

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[*] Homans, *loc. cit.*

[†] Wunderlich, *Arch. d. Heilk.* 1860, p. 219.

[‡] Valenta, Virchow and Hirsch's *Jahresb. f.* 1869, Bd. ii. p. 149.

[§] Braun, *Allg. Wien. med. Zeitung*, 1863, p. 281.

[‖] Pleischl and W. Folwarczny, *Zeitschrift d. kk. Gesellschaft d. AA. zu Wien*, 1858, pp. 605 and 622.

[¶] Huppert, *Arch. d. Heilkunde*, 1864, p. 254.

[**] Oppolzer, Schmidt's *Jahrbb.* 1860, Bd. cvii. p. 34.

The urine always contains bile pigment, and as a rule gives a marked reaction with nitric acid. In a very few cases it has happened, as is sometimes the case in ordinary jaundice, that the urine, though staining linen and having a yellow froth, yet has given no Gmelin's reaction.[*]

In some of the reports it is stated that the bile acids were absent, and in others that they were present in considerable quantity; in one case in such abundance as to be detected at once by Neukomm's modification of Pettenkofer's tests.[†] It does not appear to me, however, that in most of these cases the bile acids were searched for, and separated out from the rest of the urine; and until this have been done, nothing whatever can be predicated of the presence or absence of bile acids in the urine. Petersen, however, in Rehn's case carefully separated the bile acids from the rest of the urine, and successfully tested their presence with Pettenkofer's test.[‡] An attempt was made to estimate the amount in Huppert's; but as he remarks that the body weighed was by no means pure, the figures seem to me valueless.[§]

Since Frerichs first drew attention to their presence in the urine of acute yellow atrophy, leucin and tyrosin have been often looked for, but with various methods and various results. The methods used are by no means alike. Some have used a very simple plan; they have allowed the urine to settle and collected the sediment; or they have evaporated the urine and examined the crystals formed. In both cases the test has been the shape and arrangement of the crystals seen under the microscope. Few tests are, however, more deceptive; there are many constituents of the urine which give an appearance easily to be mistaken for leucin or tyrosin: such, for example, as urate of soda and ammonia. The only way in which these bodies can be recognised is by separating them from the urine and applying tests to the crystals. Frerichs, Hoppe-Seyler, Scherer, Dr. Arthur Gamgee, and Schultzen and Riess, have all, more or less, recognised the need of this separation, although varying methods for purification have been employed.

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[*] Riess, *loc. cit.* Concato, *Annali universali di Med.* 1861, Vol. clxxvii. p. 6 Schmeisser, *loc. cit.*

[†] Rosenstein, *loc. cit.*

[‡] Rehn, *Berlin: klin. Woch.* 1875, p. 650.

[§] Huppert, *Arch. d. Heilk.* 1864, p. 254.

Although tyrosin has been so often looked for, yet it seems to me that no proof of its existence in the urine of acute yellow atrophy was offered until the observations of Schultzen and Riess were published. In Bamberger's case, Scherer failed to find tyrosin; and the tests spoken of by Frerichs, by Hoppe-Seyler in Sander's case, and by Dr. Arthur Gamgee fail in certain particulars, although it must be owned that Frerichs' account comes the nearest to demonstration.

Schultzen and Riess evaporated the urine to one-third of its bulk, and collected the crystals which formed after 24 hours. These crystals, weighed after drying at 100° C. were over 3 grammes from 900 C.C. of urine, and from an elementary analysis gave the same proportion of carbon, hydrogen, oxygen, and nitrogen, which tyrosin does. Next after warming a little of the body with concentrated sulphuric acid, and diluting with water and carbonate of baryta until the acid reaction disappeared, the filtrate took on with chloride of iron a dark violet appearance. (Piria-Städeler's test.)

In like manner after boiling this body with nitrate of mercury, to which a drop of fuming nitric acid had been added, a rose red colour appeared, which after some time threw down a yellow red precipitate. (Hofmann's test.)

From these reactions Schultzen and Riess think there can be no doubt of the identity of this body with tyrosin.* Scherer, and Prof. Maisch, in Dr. H. C. Wood's case, could find no tyrosin, though it seems to have been carefully looked for. Both these observers say that they found leucin.

Scherer seems to have been the first really to verify the presence of leucin in the urine of acute yellow atrophy. Frerichs says he found it in large quantity, but does not give his method of testing; so also Dr. Arthur Gamgee.

Schultzen and Riess have carefully sought for leucin in the urine by the following method. The liquid which remained after the first crystallization for tyrosin was again evaporated, and the mass of crystals washed with cold dilute spirit. After repeated crystallization leucin was found in a perfectly pure state. It was more than 2 grammes in weight (out of 900 C.C.), but much was lost. For proof of its identity with leucin, the body partly sublimed in a glass tube by means of heat, and partly decomposed, carbon and amylamin being formed. A little also being evaporated with nitric acid in a Berlin dish showed, when warmed with caustic soda, a peculiar oily fluid. (Scherer's test.)

Some observers report that there was no leucin or tyrosin in the urine of their cases. In the majority this merely means that there was no sediment in the urine which under the microscope showed crystals like either of these bodies. Petersen, however, who seems to have made a careful analysis of his cases, found no leucin or tyrosin.

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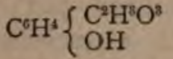
* Schultzen and Riess, *Annalen des Charité Krankenhauses*, Berlin 1869, Bd. xv. p. 71. To show how easily urate of ammonia may be mistaken for tyrosin, they say they found in the mother liquor a body under the microscope very like tyrosin, but which gave off ammonia when treated with potash, and on adding hydrochloric acid, uric acid crystals were formed which also gave the murexid reaction.

Schultzen and Riess likewise found in the urine a body like peptone. The urine was first evaporated in a water bath, and, while yet warm, mixed with spirit 95 *per cent.* strong. A considerable precipitate was caused in this way, which after standing showed itself as a dark brown mass adhering closely to the dish. The whole was put into a flask of proper size, boiled, and alcohol added so long as a precipitate was formed. After 24 hours the spirituous solution could be poured off quite clear while the precipitate clung to the walls of the vessel. This precipitate easily dissolved in water, with the exception of a brown powdery matter at the bottom, and formed a slightly opalescent dark brown solution, in which alcohol caused an abundant precipitate. By repeated precipitation with alcohol and solution in water, and finally washing with æther, a grey yellow powder, hygroscopic, was obtained. It had the following properties: in water easily soluble and the solution almost colourless, and neutral to test paper; in æther and alcohol absolutely insoluble; nitrate of mercury and nitrate of silver throw down the watery solution, and the precipitate slowly redissolves in excess of nitric acid; subacetate of lead causes a considerable cloudiness; heated on platinum foil, the body is burnt off with smell of horn, leaving scarcely any residue; tested with potash and oxyde of iron, abundant nitrogen is given off: no sulphur can be found. From these reactions there could be no doubt that a peptone was present.

The bodies remaining in solution in the first alcoholic washing were also examined; the spirit was driven off and a syrup left behind which was exhausted with æther. The æthereal extracts were added to one another and evaporated, and a brown thin fluid residue was left from which long colourless needles and brown oily drops separated. Water dissolved the crystals easily, but the oily drops remained undissolved and could be filtered off. In the yellowish coloured filtrate a solution of sugar of lead caused a slight precipitate by which the colouring material was completely removed. By removal of the lead with sulphuretted hydrogen and repeated crystallization, a body was obtained which Schultzen and Riess[*] consider to be oxy-phenyl-glycollic acid the formula of which is:



$$C^6H^4\begin{cases}C^2H^3O^3\\OH\end{cases}$$

and which bears the same relation to phenyl-glycollic acid that oxybenzoic acid does to benzoic acid.

The æthereal extract also contains sarcolactic acid, which is got by treating the filtrate from the lead precipitate with sulphuretted hydrogen, filtering off the sulphide of lead, and evaporating: the fluid must be warmed over a water bath till all the acetic acid be driven off, then the sarcolactic acid remains behind, and forms a colourless, highly acid, syrup, which is best changed at once into a zinc salt.

It is stated by Pleischl and Folwarczny that sugar was present in the urine of their second case; Schultzen and Riess say it is never found.

Neither Scherer nor Schmeisser found hippuric acid in the urine of acute yellow atrophy.

According to Schultzen and Riess, blood corpuscles are often found in the urine of acute yellow atrophy. They are not, however, often spoken of in the reports.[*] Hæmaturia to such an extent as to draw special attention seems uncommon.

The presence of casts is very commonly indeed spoken of. They are of all kinds, hyaline, epithelial, and granular, and are accompanied by epithelial cells apparently from the kidney. In some few cases they have not been found when looked for, but it would appear to be the rule that they are found if search be made for them.

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[*] I suppose, at least, this is the right name: "Mandelsäure" is, I am informed, phenyl-glycollic acid, so "Oxy-mandelsäure" ought to be oxy-phenyl-glycollic acid.

[†] See p. 456.

To sum up: a thorough investigation of the urine in acute yellow atrophy has yet to be made; it would appear probable that in some cases the urea disappears, or is in very small quantity, although in others it is said that it is increased; that the inorganic salts, the phosphates, and especially the chlorides, are sometimes decreased; that albumen is present as a mere cloudiness, after boiling and adding nitric acid, in ordinary cases, though instances have been made known in which a large quantity of albumen was present; that leucin and tyrosin may be present, although I am far from endorsing Schultzen and Riess' statement that leucin and tyrosin are as pathognomonic for acute yellow atrophy as albumen for Bright's disease, or sugar for diabetes; that a peptone and sarcolactic acid and oxy-phenyl-glycollic acid may be found in the urine, as Schultzen and Riess have demonstrated these bodies in their cases of acute yellow atrophy; that the urine is always of a bilious colour from the presence of bile pigment; that the presence of bile acids has, in a very few cases, been shown; and that casts, hyaline, granular and epithelial, are not uncommonly found.

The disappearance of the urea from the urine together with the inorganic salts, taken together with the appearance of leucin and tyrosin, and, according to Schultzen and Riess, of a peptone, is a matter of the very deepest interest. In the present state of physiology the place where the urea is formed is most uncertain, but the disappearance of urea from the urine leaves no room for surprise in a pathological state where every gland and every muscle is found acutely degenerated. It is interesting to observe the appearance of lower grades of tissue metamorphosis, such as leucin and tyrosin, in the urine which some physiologists seem inclined to believe are early steps in the every-day change of albumen into urea.

The Blood. Buhl seems to have been the first to look at the blood through the microscope. After death he found that the blood in the *vena cava inferior* and right auricle held such a quantity of colourless corpuscles that they seemed to be more numerous than the red.* Bamberger soon after repeated the observation, five days before death, and found in proportion many colourless corpuscles.† In one of Klob's cases the blood after death showed a slight increase of the white elements. They had a finely granular appearance, and Klob estimated the proportion of the white to the red as 1 in 60 in arterial blood and 1 in 25—30 in the hepatic vein.‡ Rosenstein found a very considerable increase of white corpuscles in the blood taken about 12 hours before death. In the field of the microscope were seen 60 to 70 white corpuscles, while with healthy blood only 8—10 ought to be seen.§ In like manner Matterstock found an increase of white corpuscles in his two cases; in the first 80 were seen in the field, in the second 20 to 30.||

Bergeron, on the other hand, found during life no change in the number of the white corpuscles.¶ Dr. Grainger Stewart examined the blood in the liver but does not speak of any increase of the white corpuscles;** so Dr. H. C. Wood.†† Picot found no increase of the white

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* Buhl, *Zeitschrift f. rat. Med.* 1854, N.F. Bd. iv. p. 353.

† Bamberger, *Verhandlungen d. phys.-med. Gesellschaft in Würtzburg*, 1858, Bd. viii. p. 270.

‡ Klob, *Wien. med. Wochenschrift*, 1865, p. 1360.

§ Rosenstein, *Berlin. klin. Wochenschrift*, 1868, p. 161.

|| Matterstock, *Wien. med. Wochenschrift*, 1876, p. 882.

¶ Bergeron, *Union méd.* 1862, t. xiv. p. 565.

** Grainger Stewart, *op. cit.* p. 325.

†† H. C. Wood, *op. cit.*

corpuscles, but he found in the blood drawn by a syringe from the brachio-cephalic vein the following characters: The liquid presents a greenish tinge and the red globules have diminished to an astonishing extent; that is to say, that only thirty or forty are seen in the field of the microscope; no bacteria are met with nor any coloured crystals.* Rosenstein describes the red corpuscles in his case as for the most part well preserved; some were shrunken, jagged, with the stroma quickly becoming granular. In three or four red corpuscles there were distinct changes of shape, such as the sending out of two or three projections and constrictions in the middle.† Matterstock has carried these observations of Rosenstein's much farther. He describes the changes which the red corpuscles undergo under two heads; one, in which the shape of the corpuscle resembles a mulberry; the others, in which the shape of the corpuscle becomes stellate. It is plain that the stellate form is only an exaggerated phase of the mulberry-shaped corpuscle. The projection in one is pointed, in the other round. Of these projections Matterstock has counted from 4 to 18 on the circumference of one corpuscle. No movement or constriction could be seen. Upon the surface the corpuscles were marked with points corresponding in number to the projections from the circumference. The points on the surface were, like the projections, in all cases dark, sharply circumscribed, and like granules in appearance. They were much sharper in outline than those indentations caused by chemicals on natural blood corpuscles. By the side of these changes were seen also those which take place in healthy blood when it is allowed to cool or evaporate.

Matterstock does not insist that these changes take place in the living circulation, but he thinks it noteworthy that such appearances should be seen so soon after withdrawal from the vessels. They could not be due to temperature, whether high or low, as the thermometer only varied between 35° and 38·5° C. (95° to 101° ·4 F.) Chemical influences may be set aside, for the action of the bile acids is quite different to this, although Matterstock remarks that the urine of his second case added to healthy blood caused precisely the same changes as those which were seen in the diseased blood. A patient dying with uræmia showed perfectly natural red corpuscles.

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* Picot, *Journal de l'Anatomie et de la Physiologie*, 1872, t. viii. p. 252.

† Rosenstein, *loc. cit.*

All things considered, Matterstock himself inclines to the belief that the appearances are due to the same causes as the appearances described by Hüter and others in pyæmia; and that these corpuscles are like those which contain monads.* This of course opens up the whole question of the germ theory of disease, and it will only here be remarked that Waldeyer† and Zander‡ as well as Klebs and Eppinger§ have found bacteria in the bodies of those dying of acute yellow atrophy.

The chemical analysis of the blood has been directed chiefly to one or two points; the presence of leucin and tyrosin and of urea. Frerichs pointed out that the blood held considerable quantities of urea and also of leucin.‖ Scherer also found abundance of leucin in the blood of the right side of the heart and pulmonary artery, but only a little in the blood from the left side.¶ Tyrosin was found nowhere. In like manner Kletzinsky found no tyrosin in Pleischl's case.[*] Folwarczny found much leucin in the blood of the inferior vena cava in Standhartner's case, but nothing is said of tyrosin.[†] On the other hand Schultzen and Riess, analysing 8 ounces of blood drawn from a vein during life, found no leucin after a careful search, but crystals of tyrosin separated out, and were recognised as such by Hofmann's test.[‡]

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* Matterstock, *op. cit.* p. 909.

† Waldeyer, *Arch. f. path. Anat.* 1868, Bd. xliii. p. 533.

‡ Zander, *ibid.* 1874, Bd. lix. p. 153.

§ Eppinger, *Prager Vierteljahrsschrift*, 1875, Jahrg. xxxii. Bd. i. p. 32.

‖ Frerichs, *op. cit.* Bd. i. pp. 217 and 221.

¶ Scherer, *Verhandlungen der phys.-med. Gesellschaft in Würtzburg*, 1858, Bd. viii. p. 283.

Sander could find no urea nor carbonate of ammonia in the blood of his first case.[§]

Kletzinsky analysed at length the blood taken in a bleeding from one of Pleischl's cases. There was a rather voluminous clot, and the serum contained urea in very small quantity; biliphæin abundantly, and much cholestearin. No bile acids, acetic acid, uric acid, or sugar could be found. The following percentage is given:

Water	92·135	
Albumen	5·134	Scarcely normal.
Extractives	·583	
Fatty matters	·391	Much cholestearin.
Fatty soap	·234	Palmitate of soda.
Alkaline salts	1·471	Much chlorides and phosphates, but little sulphates and earthy phosphates.[‖]

Picot analysed 97 grammes of blood taken from the body after death; it was dried and then extracted with æther for two days; it was then filtered, and allowed to evaporate spontaneously. The residue was treated with 150 grammes of boiling alcohol, and immediately filtered and left to evaporate. Crystals very like cholestearin were seen. These dried and weighed gave ·175 grm. of cholestearin, that is, about 1·804 in the 1000.* According to Picot, blood from the urine of a healthy man only holds ·625 of cholestearin in 1000. Huppert found no bile acids in the blood taken after death from the heart and lungs.†

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[*] Pleischl, *Wien. med. Wochenschrift*, 1855, p. 20. Wertheimber (*Fragmente zur Lehre des Icterus*, München, 1854, p. 31) detailing apparently the same case, says that tyrosin was present; "tyrosin, an organic sulphur."

[†] Standhartner, *Zeitschrift d. kk. Gesell. der AA. zu Wien.* 1858, p. 787.

[‡] Schultzen and Riess, *Annalen d. Charité-Krankenhauses*, 1869, Bd. xv. p. 85.

[§] Sander, *Deutsche Klinik*, 1860, p. 34.

[‖] Pleischl, *loc. cit.*

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* Picot, *op. cit.* p. 255.

† Huppert, *Arch. d. Heilk.* 1864, p. 255.

CHAPTER XXI.

THE MORBID ANATOMY AND PATHOLOGY OF ACUTE YELLOW ATROPHY.

THE body, at the time when it is offered for examination, may show no marks whatever of decomposition, or may be far advanced in putrefaction, and this without any regard to the time passed between death and the hour of examination. In other kinds of jaundice my own experience teaches me that putrefaction more commonly sets in rapidly than not; but on this point I should like to draw the attention of observers to the high temperature which precedes death in some cases, with a view to the making sure if the high temperature and rapid decomposition be coincident. Lebert speaks of the rapid decomposition as having been noticed by himself* and others in rapidly fatal jaundice.

The jaundice may be very deep, and it may pass through all degrees of intensity until it become so slight that it may only be noticed after death, although this is rare.

In some few cases the substance of the brain, as distinguished from the meninges and pia mater, is said to be yellow.† This is, however, but rarely stated; and must be received with a certain amount of hesitation, as it is contrary to what is seen universally in other cases of jaundice.

No changes in the brain of any great importance have hitherto been found by any considerable number of observers in acute yellow atrophy. The greater number of reports certainly say that the brain is quite natural. Yet in a large number, changes are spoken of, but without any degree of agreement as to what the changes are. In several cases the brain is said to be full of blood;[*] and in others, the grey matter to be pink. In others just the contrary is stated; the brain is said to be bloodless, and the grey matter pale. In other cases the brain is noted as soft, and on the other hand in one case[†] the brain is said to be tougher than natural. In others, chiefly from Vienna, the brain is said to be moist and soft.

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* Lebert, *Arch. f. path. Anat.* 1854, Bd. vii. p. 350.

† Valenta, Virchow and Hirsch's *Jahresbericht f.* 1869, Bd. ii. p. 149.

In only two cases can I find any examination of the brain with the microscope. Pleischl and Folwarczny found the brain in one of their cases swollen, with abundance of pus cells and nuclei on examination with the microscope.[‡] Steiner, in his case of a boy of 10, found important changes in the walls of the capillaries, best described under the name of cloudy swelling.[§]

Oppolzer found in a case that the vessels of the brain were fatty, but this was seen in the vessels of other parts as well.[||] Mr. Robinson reports that in a case of a syphilitic drummer boy, the vessels of the brain "showed evidence of inflammation."[¶]

Hæmorrhages are now and then found in the meninges and substance of the brain. They appear to be parts of the general hæmorrhagic diathesis. Thus, Rosenstein found in the right *corpus striatum* a hæmorrhage the size of a nut;[**] and Klob,[††] Politzer,[‡‡] and Fritz[§§] and

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[*] See Riess' two cases (*Annalen der Charité*, 1865, Bd. xii. Heft ii. p. 122) in which there was marked hyperæmia of the brain, and von Krafft-Ebing's case (Virchow and Hirsch's *Jahresbericht f.* 1871, Bd. ii. p. 161) in which the soft parts within the skull were hyperæmic, and the cortex of brain violet-grey from hyperæmia.

[†] Buhl, *Zeitschrift f. rat. Med.* 1854, Bd. iv. Neue Folge, p. 352.

[‡] Pleischl and Folwarczny, *Wien. med. Zeitschrift*, 1858, p. 605.

[§] Steiner, *Jahrb. f. Kinderheil.* 1871, Bd. iv. Neue Folge, p. 228.

[||] Oppolzer, Schmidt's *Jahrbb.* 1860, Bd. cvii. p. 34.

[¶] Robinson, *Trans. of the Path. Soc. of London*, 1865, Vol. xvi. p. 152.

[**] Rosenstein, *Berlin. klin. Wochenschrift*, 1868, p. 161.

[††] Klob, *Wien. med. Wochenschrift*, 1865, p. 1357.

[‡‡] Politzer, *Jahrb. f. Kinderheilkunde*, 1860, Bd. iii. p. 40. See also same journal, 1859, Bd. ii. p. 42 for hæmorrhage in a child 1½ years old.

[§§] Fritz, *Gaz. des Hôp.* 1863, p. 81.

Kuhn[*] found meningeal hæmorrhages. Monneret appears to have been the first to notice the appearance of hæmorrhage into the meninges, but in one of his cases no change was found by Robin in the liver; and in the other, the liver cells were merely infiltrated with fat.[†] Bazin noticed the presence of blood between the dura mater and the skull in a case not made certain by examination with the microscope after death,[‡] and in one of Degen's cases the dura mater itself showed numerous ecchymoses.[§]

Picot has had the brain analysed with a view to estimating the amount of cholestearin. He found 1·52 *per cent.* whereas in the natural state there should only be ·9593 *per cent.* He thinks therefore that this analysis rather favours the view of Dr. Austin Flint.[||] Liebermeister reports a case in which the brain was examined in Hoppe-Seyler's laboratory and found to contain a great excess of fat.[¶]

Dr. Shingleton Smith has examined with the microscope the superior cervical ganglion of the sympathetic, and found a shrunken and granular appearance of the cells. This observer himself, however, thinks it possible that the changes seen in the ganglion may be due to the action of the preservative fluid in which the ganglion had been kept; an opinion which I am myself prepared to endorse.[**]

The pleuræ very often show numerous ecchymoses both on the parietal and visceral layer, though not so commonly as on the pericardium or peritonæum. The lungs as a rule show no morbid appearances; in a few of the early cases, mention is made of hæmorrhagic infarcts, and of pneumonia. In a case of Chaumel's, in which parotid bubo and symptoms of purulent infection complicated the disease, metastatic abscesses were found in the lungs.[*] In two cases the presence of tubercles has been noted. It may be remarked that it is strange that they have not been seen more often.

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[*] Kuhn, *De atrophia hepatis acuta*, Diss. Inaug. Viadrina, 1859, p. 26.

[†] Monneret, *de l'ictère hêmorrhagique esssentiel*, Paris, 1859, pp. 8 and 10.

[‡] Bazin, *Gaz. des hôp.* 1862, p. 489.

[§] Degen, *Zur Lehre von d. akuten Leberatrophie*, Diss. Inaug. Erlang. Nürnberg 1865, p. 21.

[||] Picot, *Journal de l'Anatomie*, 1872, p. 261.

[¶] Liebermeister, *Beiträge zur path. Anat. u. Klinik der Leberkrankheiten*, Tübingen, 1864, p. 191.

[**] R. Shingleton Smith, *Brit. Med. Journal*, 1878, Vol. ii. p. 170.

Under the microscope, the epithelium shows itself granular, desquamating and lying loose in the cavity of the alveoli.[†] The epithelium of the bronchi and air passages were found overladen with fat in one of Wunderlich's cases.[‡]

The pericardium and endocardium are very commonly indeed the seat of ecchymoses and larger hæmorrhages. In fact, with the peritonæum and omentum, they are the favourite seat of petechiæ in this disease.

The heart shows very important and extensive alterations. The earliest observers[§] were contented to notice the flabbiness, pallor, and shrunken state of the walls. Even Frerichs seems to have paid but little attention with the microscope to this organ, although Buhl, as a necessary part of his theory, had shown in 1857 that the fibres were in a state of fatty degeneration,[‖] and his observation was soon after confirmed by Pleischl and Folwarczny,[¶] Klob,[**] and very many others, so that there no longer remains any doubt that in a large proportion of cases of acute yellow atrophy the muscular fibres of the heart are in a state of acute fatty degeneration. Thus, out of thirty-four cases in which the heart fibres were examined with the microscope, I can only find four in which they are reported to be natural. In those reported to be changed, the disease was in every case of the same kind; a granular infiltration of the muscular fibres. In some cases this is reported to be small in amount and affecting only a few of the fibres, but it passes, from this small amount of disease, through all stages, until at last a complete destruction of the structure be reached.

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[*] Chaumel, *Gaz. des hôp.* 1863, p. 308.

[†] Eppinger, *Prag. Vierteljahrsschrift*, 1875, Bd. i. p. 32.

[‡] Wunderlich, *Arch. d. Heilkunde*, 1863, Jahrg. iv. p. 149.

[§] Horaczek, *Die gallige Dyscrasie*, Wien, 1843, pp. 90, 98 and 119.

[‖] Buhl, *Zeitschrift f. rat. Med.* 1857, Bd. viii. Neue Folge, p. 38.

[¶] Pleischl and Folwarczny, *Wien. med. Zeitschrift*, 1858, p. 605.

[**] Klob, *Zeitschrift d. kk, Gesellschaft der Aerzte zu Wien*, 1858, p. 736.

Disease of the valves of the heart does not seem to be very common. Dr. Goodridge found in his case that the mitral valve showed a fringe of minute soft, red vegetations. The sigmoids were natural.[*] In one of Riess' cases the heart was found large, with the mitral and tricuspid valves thickened.[†] In one of Degen's there was some amount of mitral stenosis, of old standing.[‡] And Dr. Handfield Jones found small fibrinous fringes on the aortic valves.[§] De Roquetaillade has noticed in a woman aged 32 the destruction of the liver cells coinciding with disease of the aortic and pulmonary valves, and has devoted a thesis to the consideration of the complication of jaundice and endocarditis.[‖] He seems to think that the endocarditis is a sequence of the grave general state of the acute yellow atrophy.

It is a matter for regret that hitherto but little attention has been paid to the state of the voluntary striped muscles at large. Paulicki found the pectoral muscles in a state of granular degeneration like those of the heart,[¶] and Dr. Coats a similar change in the muscles of the thigh.* Schultzen and Riess found the muscles all over the body degenerated.† So also Wunderlich.‡ But Moraud found no change in the *rectus abdominis.*§ The heart is probably the first to suffer in this disease, and the voluntary muscles last; but in observations to be hereafter made, it will be an important point to note if the whole of the muscular, as well as the epithelial, system suffer, for it is probable that the muscles, equally with the glands, are the seat of a destructive change.

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[*] Goodridge, *British Medical Journal*, 1871, Vol. i. p. 609.

[†] Riess, *Annalen d. Charité*, 1865, Bd. xii. Heft. ii. p. 122.

[‡] Degen, *op. cit.* p. 13.

[§] Handfield Jones, *Lond. Med. Gaz.* 1847, N.S. Vol. v. p. 1145.

[‖] J. de Roquetaillade, *Étude sur la coexistence dans les états généraux graves de l'endocardite et de l'ictère*, Thèse de Paris, 1874.

[¶] Paulicki, *Berlin. klin. Woch.* 1869, p. 47.

The spleen in former times was thought to be the organ most commonly diseased after the liver. Horaczek§ and Frerichs‖ both speak of an increase in size of the spleen as an almost essential part of acute yellow atrophy. Out of 23 cases Frerichs found the spleen enlarged in 19, small in 1, natural in 3. Liebermeister, however, showed that the swelling of the spleen was by no means so constant; for in 31 out of 87 cases the spleen was found natural or smaller than usual.¶ In my own collection, from which doubtful cases were expunged, I found that in 43 the spleen was enlarged sometimes slightly, sometimes to double its size; in 23 the spleen was natural in size, and only in 5 was it below normal. This is very close to the proportion given by Liebermeister. With the increase of size a loss in the firmness of the organ is usually noted, and *vice versâ.*

The cause of the swelling of the spleen is very obscure. Liebermeister thinks the amount of swelling to be very likely dependent upon the length of the disease, just as he has shown that the liver is often large or small according to the day of the disease. He thinks that the spleen enlarges as the disease goes on, and the liver decreases. It seems most probable that the swelling of the spleen is due to the same cause as in the pyrexial disorders.

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* Coats, *British Med. Journal,* 1875, Vol. i. p. 847.

† Schultzen and Riess' *Annalen des Charité-Krankenhauses,* Berlin, 1869, p. 67.

‡ Wunderlich, *Arch. d. Heilkunde,* 1863, Jahrg. iv. p. 149.

§ Moraud, *Gaz. des Hôp.* 1873, p. 154.

§ Horaczek, *op. cit.* p. 21.

‖ Frerichs, *Klinik d. Leberkrankheiten,* Braunschweig, 1858, Bd. i. p. 234.

¶ Liebermeister, *Beiträge zur path. Anat. und Klinik d. Leberkrankheiten,* Tübingen, 1864, p. 231.

Frerichs thinks that the absence of swelling is due in all cases to the spleen being bound down by thickenings of the capsule, or to profuse bleedings from the roots of the portal vein. This does not seem to be borne out by the observations of Liebermeister just spoken of.

The peritonæum is very commonly indeed the seat of multiple ecchymoses. It rarely escapes, and the omentum is a favourite place to be seized on. The endothelium of the serous membranes and of the vessels was found by Wunderlich to share in the general fatty degeneration of the rest of the cells.*

Dr. Murchison records a case in which the peritonæum was the seat of an acute but slight inflammation.†

The stomach commonly holds a black or brownish fluid, which the microscope shows to be altered blood. Occasionally, but not often, it holds fluid which may be asserted with the naked eye to be blood, and in some cases in large quantity; Homans speaks of a quart.‡ The same contents extend through the intestinal canal in many instances, but they become thicker and more tarry in consistence as they pass downwards towards the anus. In others the fæces, uncoloured by bile, so commonly seen in jaundice, are found. Very rarely indeed, are the contents of the intestine of a natural brown colour.

The stomach and intestines often show abundance of ecchymoses, rarely however, very large. The glands of the stomach appear to have been examined in only two instances, once in one of Traube's two cases by Cohnheim,* and again by myself.† In both cases the glands were found filled with a highly granular and disintegrating epithelium; a state analogous to that of the other glands of the body. It is somewhat surprising that so few observations should have been made when the state of the glands of the stomach in poisoning by phosphorus is so well known.

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* Wunderlich, *Arch. d. Heilkunde*, 1863, Jahrg. iv. p. 149.

† Murchison, *Trans. of the Path. Soc. of Lond.* 1868, Vol. xix. p. 248.

‡ Homans, *Boston Med. and Surgical Journal*, 1871, Vol. viii. New Series, p. 305.

The stomach and intestines commonly show the appearances of a chronic catarrh without ulceration: in my own case, there was a small ulcer covered with a clot of blood in the duodenum. The ulceration had probably begun in an ecchymosis.

Buhl‡ and Waldeyer§ have recorded a swollen state of the mesenteric glands. Horaczek reckons these amongst the most constant of the anatomical appearances,‖ but he does not appear to have been followed in this statement by many later observers. Dr. Tuckwell speaks of these mesenteric glands being swollen and reddened in a boy aged 4 years and 10 months,¶ but it is somewhat difficult to be sure that the mesenteric glands in children exceed their natural size. The same appearances were noticed in a child of one year and nine months;** but I do not think much weight is to be laid upon them.

The pancreas has been examined in two or three cases;

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* Traube, *Gesam. Beiträge*, Berlin, 1871, Bd. ii. p. 815. It is worthy of note that the man has taken antimony.

† Duckworth and Wickham Legg, *St. Bartholomew's Hosp. Reports*, 1871 Vol. vii. p. 210.

‡ Buhl, *Zeitschrift f. rat. Med.* 1854, Bd. iv. Neue Folge.p. 353.

§ Waldeyer, *Arch. f. path. Anat.* 1868, Bd. xliii. p. 536.

‖ Horaczek, *Die gallige Dyscrasie*, Wien, 1843, p. 9.

¶ Tuckwell, *St. Bartholomew's Hosp. Repp.* 1874, Vol. x. p. 42.

** *Jahrb. f. Kinderheilkunde*, 1859, Bd. ii. p. 42.

by Valenta[*] and by Mann;[†] and in each case the epithelium of the acini of the glands was found fatty or replaced by a granular detritus. In a curious case of Waldeyer's the pancreas, like many other organs, was found pigmented with black-blue spots, which spots, after being cleared up by hydrochloric acid, showed themselves to be the homes of colonies of bacteria. In the pancreas these were placed between the acini of the gland in the connective tissue.[‡]

For the first minute[§] account of the kidneys in this disease we seem to be indebted to Dr. Handfield Jones. He found the epithelium coarse and granular, and compared the appearances to those seen in scarlet fever, and asserted that the processes in the liver and kidney were identical.[‖] Since that time the kidneys have been found, with scarcely an exception, when the disease has been looked for,[¶] in a state of parenchymatous degeneration. Frerichs complained that in his time the kidneys had not received that attention that they ought,[**] a complaint which now-a-days can no longer be made.

The kidneys in acute yellow atrophy are found enlarged, the capsule separating readily, and leaving a smooth surface. The kidney itself is jaundiced like most of the tissues in this disease. The cortex is broadened, opaque, and the natural striation is lost. This change in the cortex may vary from the slightest amount of cloudy swelling to a well-marked Bright's disease. The pyramids vary from pink to purple in colour. In some cases the kidneys show to the naked eye very little change. Under the microscope, however, they all show the same appearance, varied only in degree. The tubules are filled with an epithelium containing large numbers of granules, some soluble, others not, in acetic acid. These granules may be so abundant as to obscure the nucleus or render it invisible. In later stages fat drops appear in the cells, and the contents of the tubes at last form little more than a granular and fatty detritus, in which only a few fatty epithelium cells can be made out.

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[*] Valenta, Virchow and Hirsch's *Jahresb. f.* 1869, Bd. ii. p. 149.

[†] Mann, *Annalen d. Charité*, 1863, Bd. x. Heft. ii. p. 109.

[‡] Waldeyer, *op. cit.* p. 538.

[§] It is worthy of note that Cheyne (*Dublin Hosp. Reports*, 1818, Vol. i. p. 273) while failing to find any disease in the liver, noticed some disease of the kidneys, which he describes as much enlarged, and marbled with none of the original structure to be distinguished.

[‖] Handfield Jones, *Lond. Med. Gaz.* 1847. New Series, Vol v. p. 1145.

[¶] In two of the newer cases the kidneys are stated to be natural (v. Krafft-Ebing, Virchow and Hirsch's *Jahresb. f.* 1871, Bd. ii. p. 162, and Lewis Mackenzie, *Brit. Med. Journ.* 1874, Vol. ii. p. 107) but it does not appear evident that the microscope was used in either: in Dr. Mackenzie's case the urine, not albuminous, contained hyaline casts and epithelium.

[**] Frerichs, *op. cit.* Bd. i. p. 235.

The intertubular tissue seems to have drawn little attention; in the second of Riess' cases the interstitial tissue showed many corpuscles.*

Zander found bacteria in a case of acute yellow atrophy, both in the liver and kidneys. Of cylinders and epithelial cells not a trace could be made out; larger or smaller drops of fat, or fragments of tissue with no distinguishing marks, were seen in the field, and between them, bacteria in active movement. The preparations taken from the pyramids showed the largest amount of bacteria, and these were of extraordinary length, so that the greater part of the field was taken up by them.†

The mucous membrane of the pelvis of the kidney may show numerous ecchymoses, an appearance very commonly spoken of; so also the mucous membrane of the bladder may be studded with isolated hæmorrhages.‡

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* Riess, *Annalen d. Charité-Krankenhauses*, 1865, Bd. xii. Heft. ii. p. 141.

† Zander, *Arch. f. path. Anat.* 1874, Bd. xlix. p. 155.

‡ Schultzen und Riess, *Annalen d. Charité-Krankenhauses*, 1869, Bd. xv. pp. 65, 79 and 83.

The uterus and its appendages may be found quite in the natural state or showing the appearance common after delivery or abortion. It is not unusual for the cavity of the uterus to hold blood in various stages of decomposition. In one case the hæmorrhages extended to the ovum. The placenta, membranes, and decidua, were studded through their whole thickness with small ecchymoses and extravasations of blood, and on the upper surface they were so numerous as to be confluent. There were ecchymoses on the scalp of the fœtus, and on the right side of its neck.*

I have purposely left to the last the organ which of all others has been considered the most important. I mean the liver. The state of this viscus has given a name to the disease, and more attention has been paid to it than to any other organ in the whole body. The reason of this is not far to seek. The jaundice of course led men to look to the liver; and, in disease chiefly attacking the glandular structures, the largest gland in the body would naturally be the first and chiefest to suffer: so that for a long time the liver was the only organ, save the spleen, found to be diseased. Now it is known that acute yellow atrophy is a general disorder, and that nearly all the structures in the body are involved. Still the state of the liver must be looked upon with the greatest interest.

When the body is first opened it sometimes happens that the liver is not immediately seen; the intestines, filled with air, hinder any part of the liver from coming to the surface. It is not uncommon for old adhesions between the liver and diaphragm or other parts to be present. The liver is often found so flaccid that it has fallen altogether away from the fore part of the belly and rests against the back, on the spine and the muscles attached thereto.

* Ogston, *Brit. Med. Journal*, 1873, Vol. i. p. 57.

Before the liver is taken out of the body, the capsule investing it may sometimes be seen to be thrown into folds from the great decrease in size of the organ. The liver may be large, of natural size, or greatly decreased. Liebermeister has attempted to show that the liver, early in the disease, is enlarged; but that later on it becomes small, so as to be reduced to one half or even one third of the natural weight. On taking out the organ it seems to be unnaturally soft, almost pulpy, and flaccid, so that it cannot bear up its own weight. It readily takes the print of the finger. The organ, when decreased in size, seems to suffer most in its vertical measurements. The left lobe, according to the majority of observers, is that which shows the greatest amount of decrease, and of disorganization. The colour of the organ is a bright yellow, usually mottled with red, or brownish-red tissue, hard to distinguish from the natural liver colour. See No. III. of the chromolithographs. This mottling may be seen in distinct islets of red tissue, hard and firm, depressed below the surface of the yellow, or else in much smaller masses, almost in points, and running into one another, like the red seen in nutmeg liver. Ecchymoses are sometimes seen on the capsule of the liver, and in a few rare cases, blood in substance is said to be extravasated within the liver. On cutting into the organ, the same appearances are seen as on the outside. In the greater number of cases all trace of lobular structure is lost, and the cut surface is peculiarly bloodless, dull, and devoid of its natural markings. The knife is rendered distinctly greasy.

It is important to accurately note the state of the bile ducts: in all cases of true acute yellow atrophy, no permanent obstruction to the course of the bile is found. In very many of the reports the gall ducts are said to be empty, in many others slightly stained or colourless, showing that no bile can have passed down them for some days; and in a few, a plug of mucus is spoken of at the entrance of the duodenum. The portal vein and the hepatic artery and vein are commonly found free from any disease.

The departures from the general appearances just spoken of will now be considered in detail.

i. *The colour of the liver.* In almost the first case recorded of acute yellow atrophy, Ballonius speaks of the liver as being ὑπόχλωρον, greenish yellow,[*] but the yellow colour was spoken of especially by Rokitansky[†] and in fact gave its name to the disease. It was accepted by Frerichs, who speaks of the yellow-ochre or rhubarb colour of the liver,[‡] by Förster for the second stage of the disease,[§] and by Bamberger.[‖] The majority of observers have regarded the pale, yellow, bloodless appearance of the liver as characteristic, and in fact the term "yellow" has, with universal approval, been applied to the state of the liver.

But notwithstanding this, it is noteworthy that some of the earliest observers of cases of acute yellow atrophy had noted something beyond the appearance of yellow tissue in the liver. Even if Martinet did not see this in 1817,[*] it certainly was observed by Richard Bright in 1832. In one of his cases the liver is described as being "of a brightish yellow colour with portions marked with purple or deep brown."[**] And in the notes which Zenker took of Oppolzer's lectures in 1849 the mixture of a red with the yellow is distinctly affirmed. Oppolzer says: The colour of the liver is, in consequence of the saturation with bile, gamboge, ochre, or greenish yellow. In one case it was brown, and from the brown surface projected yellow elevations of the size of pease to hazel nuts. In the nodules liver cells were found; but in the sunken brown parts they were wanting.[*]

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[*] Ballonius, *Epid. et Ephem.* Lib. ii. quoted by Bonetus, *Sepulchretum*, Genevæ, 1700, Lib. iii. Sect. xviii. Obs. 6.

[†] Rokitansky, *Handb. d. path. Anat.* Wien, 1842, Bd. iii. p. 313.

[‡] Frerichs, *Klinik d. Leberkrankheiten*, Braunschweig, 1858, Bd. i. p. 233.

[§] Förster, *Handbuch d. path. Anat.* Leipzig, 1863, Bd. ii. p. 180.

[‖] Bamberger, *Krankheiten d. chylo-poëtischen Systems*, Erlangen 1864, p. 529.

[¶] Martinet, *Bibliothèque méd.* 1819, t. lxvi. p. 350. The liver was of the colour of rhubarb, with red streaks.

[**] Bright, *Guy's Hospital Reports*, 1836, Vol. i. p. 628. Case of Keatrina Pfifrein. See also p. 626, case just preceding.

But to Zenker belongs the merit of having been the first to generalise, as well as early to note, the appearance of a red tissue in the midst of the yellow liver. As early as 1851 he noticed this in a case which he examined at Dresden, and laid the results before a scientific society in that town.[†] Soon after this date similar appearances began to be noted in Vienna,[‡] Berlin,[§] Paris,[‖] London,[¶] Edinburgh[**] and even in America[††] and Italy,[‡‡] until it become the exception to find a case in which the presence of red tissue is not noted. But the matter was very slow to get into the handbooks either of medicine or pathology, Rokitansky in his third edition[§§] and Bamberger in his second[‖‖] and Klebs[¶¶] being so far as I know the only ones to mention the appearance[***] In 1872 Zenker published a paper in which he fully discussed the subject of the presence of the red tissue, and showed that it was a very constant appearance in acute yellow atrophy.

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[*] Oppolzer, in Zenker, *Deutsches Arch. f. klin. Med.* 1872, Bd. x. p. 171.

[†] I have been unable to see this paper. Rokitansky (*Handb. d. path. Anat.* Wien, 1861, Bd. iii. p. 272) gives it as: *Jahresb. der Ges. f. Natur- u. Heilk. in Dresd.* 1858.

[‡] Klob, *Zeitschrift d. kk. Gesellschaft d. Aerzte zu Wien*, 1858, p. 736. Pleisch *ibid.* p. 608. Standhartner, *ibid.* p. 785.

[§] Sander, *Deutsche Klinik*, 1860, p. 33.

[‖] Robin, *Mém. lus à la Soc. de Biologie*, 1857, p. 16. This observation deserves special notice as it seems to have been published before Zenker's in 1858 at Dresden. Fritz, *Gaz. d. Hôp.* 1863, p. 81.

[¶] Wilks, *Trans. of the Path. Soc. of London*, 1862, Vol. xiii. p. 107.

[**] Grainger Stewart, *Edinb. Med. Journal*, 1865, Vol. xi. p. 323.

[††] Homans, *Amer. Jour. of the Med. Sci.* 1868, Vol. lvi. p. 53.

[‡‡] Concato, *Annal. Univ. di Med.* 1861, Vol. clxxvii. p. 3.

[§§] Rokitansky, *op. cit.* p. 270.

[‖‖] Bamberger, *Khten d. chylop. Systems*, Erlangen, 1864, p. 529.

[¶¶] Klebs, *Handb. d. path. Anat.* Berlin, 1869, p. 417.

[***] Liebermeister, contrary to what Zenker says, seems to me to have appreciated the difference in colour: "Stellen, die indem sonst gelbrothen bis braünlichen

The red tissue is, according to Zenker, scattered in islets throughout the yellow liver substance, but in no case does it exceed in amount this yellow tissue, as Klebs seems to believe.[*] The red parts are much firmer and tougher than the yellow, and seem more shrunken, for the yellow appear to project. The red portions are marked off sharply from the yellow, and may be of varying size from that of pease to small apples. Others describe the red as more intimately mixed with the yellow, the red nodules being of small size and running into one another. Such would appear to be the case in the chromolithograph given by Zenker. The characters seen with the microscope will be described further on.

In Riess' two cases, the colour of the surface of the liver seems to have been a dirty red, and upon this bright yellow spots; the same appearances were seen on section. In the yellow parts, there were reddish points separated by yellow zones a millimeter thick.[†] These and one or two other observations would seem to lead to the belief that Klebs is right when he says that the red tissue may sometimes be greater in amount than the yellow, contrary to what Zenker affirms.

In some cases the colour and other properties of the liver have been found perfectly natural, nor has any change been detected on careful examination with microscope. These cases will be discussed later on. In

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Gewebe sich finden, sind gewöhnlich, ... besonders weich und zeigen die Zellen im höchsten Grade des Zerfalls. (*Beiträge zur path. Anat. u. Klinik der Leberkrankheiten*, Tubingen, 1864, p. 184.) Later on he speaks of the pale patches which are raised above the rest of the liver tissue, and show but little change in their structure.

[*] Klebs, *op. cit.* p. 421.

[†] Riess, *Annalen d. Charité*, 1865, Bd. xii. Heft. ii. p. 122.

some others the colour of the liver is noted as green-yellow* or yellow-brown,† in another grey-black.‡ In another the colour is noted as almost natural, and the lobes well marked, although scarcely a single hepatic cell could be found, and the weight of the liver was greatly decreased.§

In another case the liver was of a bluish colour,‖ and in another slate coloured.¶

ii. *The size of the liver.* Martinet found the liver reduced in size,** but Abercrombie was the first to note any remarkable decrease. In his case the liver was reduced to one third of its natural volume.†† The atrophy of the liver is one of the notes of the disease in Rokitansky's description.‡‡ Still it is not necessary for the liver to be shrunken; it may even be larger than natural, or the natural size, and when smaller than natural, it may be only a little below the normal standard, or may be one half or even one third of its natural weight. The greatest shrinking of the liver that I have seen recorded is in a case of Dr. Clements. The girl was 17 years old, and yet the liver weighed only thirteen ounces avoirdupois, about 368 grammes.§§ Zimerman in a girl of the same age found the liver weighed only a *Civilpfund*, probably about an English pound or 500 grammes.‖‖ In one of Dr. Shingleton

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* Oppolzer, quoted by Zenker, *loc. cit.* Davidson, *Monatsschrift f. Geb.* 1867, Bd. xxx. p. 452.

† V. Krafft-Ebing, Virchow's *Jahresb. f.* 1871, Bd. ii. p. 162.

‡ Moraud, *Gaz. d. hôp.* 1873, p. 154.

§ Vallin, *Gaz. hebd.* 1867, t. iv. p. 487.

‖ Spengler, *Arch. f. path. Anat.* 1854, Bd. vi. p. 129.

¶ Hiffelsheim and Robin, *Gaz. méd.* 1857, p. 659.

** Martinet, *loc. cit.*

†† Abercrombie, *Pathological and Practical Researches on Diseases of the Stomach, etc.* Edinb. 1828, p. 336.

‡‡ Rokitansky, *loc. cit.*

§§ Clements, *British. Med. Journal*, 1871, Vol. i. p. 367.

‖‖ Zimerman, *Wien. med. Woch.* 1857, Jahrg. vii. p. 364. The pound now used in the German Empire is, I am informed, exactly 500 grammes.

Smith's cases, he found the weight of the liver in a grown-up woman to be only 18½ oz.[*]

In one of Homans' cases, a woman aged 28, the liver weighed only 22½ ounces; the ratio of liver weight to body weight was as 1 : 117·33. In health it is 1 : 36.[†] In another case, a lad of 18, the liver weighed 24 oz.[‡] It is common in acute yellow atrophy for the liver to weigh below two pounds avoirdupois or 1000 grammes.

In many of the earlier cases the liver is said to be natural in size, and in a case recorded by Budd the liver is noted as rather large, and weighed four pounds four ounces,[§] about 1867. grammes, though of course this falls within the limits of health as determined by Frerichs. Lebert also early noticed that the more intense and rapidly fatal the jaundice, the less marked was the shrinking of the liver.[||] Wunderlich in 1860 noted a liver which he says was twice above the natural size, and the same weight as Budd's.[¶] But Liebermeister was the first to attempt to establish as a general principle that a swelling of the liver goes before the shrinking. He thinks it not unlikely that, if in parenchymatous nephritis a swelling of the kidney precede the decrease in size, the same may happen in the liver. Even in cases where the decrease in size of the liver has been most marked, Liebermeister has found the cells left behind larger than natural. Further, he collected 94 cases. In 57 the liver was much decreased: in 47 the disease had lasted 9 days: in only 10 cases less than 9 days. The others, 37 in number, in which the liver was either of natural size, or enlarged, or slightly smaller, showed only 10 in which the disease lasted more than 9 days: in 27 it lasted less than 9 days. From this it is concluded that a considerable shrinking of the liver is most commonly met with when the disease has lasted more than 9 days. The exceptions, on either side, are due either to a slow subacute form of the disease, or to a remarkably rapid course of the affection. Besides, it is often hard to determine the exact day on which the disease began.*

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[*] Shingleton Smith, *Brit. Med. Journal*, 1878, Vol. ii. p. 170.

[†] Homans, *American Journal of the Med. Sciences*, 1868, Vol. lvi. p. 53.

[‡] Homans, *Boston Med. and Surg. Journal*, 1871, Vol. viii. New Series, p. 305.

[§] Budd, *On Diseases of the Liver*, London, 1857, Third ed. p. 252.

[||] Lebert, *Arch. f. path. Anat.* 1855, Bd. viii. p. 183.

[¶] Wunderlich, *Arch. d. Heilkunde*, 1860, Bd. i. p. 218.

iii. *The consistence of the liver.* In the vast majority of cases the liver is said to be decreased in consistence, to be soft, pulpy, almost diffluent. Budd gave the name of softening of the liver to his cases,* and this decrease of consistence has never been denied, as a general appearance, until a German observer, who has attained a high reputation in this country, but one not so great in his own, called the matter into doubt, and stated that the liver was tough and leather-like.† This strange statement might be left to confute itself: but on looking through the bibliography of acute yellow atrophy I can find only four cases in which the tissue was harder or tougher than natural.‡ In some few other cases it is indeed noted that the tissue is not soft but of natural consistence. It is clear that an increased consistence is the exception and not the rule, except in the patches of red atrophy which Zenker has pointed out.

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* Liebermeister, *Beiträge zur pathologischen Anatomie u. Klinik der Leberkrankheiten*, Tübingen, 1864. p. 224 *et seqq.*

† Rindfleisch, *Lehrb. d. path. Gewebelehre*, 1871, 2te Auflage, p. 406.

‡ Hilton Fagge, *Trans. of the Path. Soc. of Lond.* 1867, Vol. xviii. p. 136. Consistence dense.

Aron, *Gaz. hebd.* 1869, p. 739. A great drunkard: liver like leather.

Jahrb. f. Kinderheilkunde, 1859, Bd. ii. p. 42.

Picot, *Journal de l'Anatomie*, 1872, viii.e Année, p. 246. Liver creaked under knife. Constitutional syphilis.

Burkart, *Ueber acute gelbe Leberatrophie*, Diss. Inaug. Tüb. Stuttgart, 1872, p. 6. Harder to cut than a sound liver.

Tuckwell, *St. Bartholomew's Hosp. Rep.* 1874, Vol. x. p. 40. Liver could be folded without tearing.

Buhl, *Zeitschrift f. rat. Med.* 1854, Bd. iv. p. 352. *Gefüge äusserst welkzäh.*

Chiari, Braun, and Späth *Klinik d. Geburtshilfe*, Erlangen, 1855, p. 245.

Liebermeister, *op. cit.* p. 186.

Waldeyer, *Arch. f. path. Anat.* 1868, Bd. xliii. p. 536.

An examination of the liver with the microscope is most important. It is absolutely necessary for the diagnosis of the disease, and may be made with great ease as soon as the liver is withdrawn from the body. A scraping from the cut surface should be placed under the microscope and examined with a high power. If any liver cells be seen they will be swollen,* filled with granules, or even with small drops of fat, so that the nucleus is obscured, or invisible; or with the liver cells may be seen an oily detritus, drops of fat, coloured rhombic crystals, and shreds of tissue covering the field. But if the disease be far advanced, no liver cells whatever may be seen, and nothing but the detritus of tissue discovered. This disappearance of the liver cells was known to Budd and other early observers, and is the outcome of the pathological process which they undergo, a parenchymatous degeneration, a change closely allied to that seen in the heart, kidneys, and other glandular structures.

Thus much was known to the earlier observers. Frerichs added a further description: he speaks of a hyperæmia of the capillaries, and an exudation of a dirty grey yellow mass between the lobules. Later on the hyperæmia disappears, the size of the lobules becomes less, and the exudation gains the upper hand.† Foerster appears to be one of the few observers who follows Frerichs in his account of a hyperæmia and exudation,* but the belief that the process was most active in the circumference of the lobules gained ground. and has been accepted by Bamberger† and other observers. One of the earlier observers, however, of this disease found the cells at the margins of the lobules still existing, while in the other parts, they were reduced to a detritus.‡ Dr. Grainger Stewart§ and Dr. Christy Wilson of Edinburgh,§ Schultzen and Riess,|| with others,¶ agree with Frerichs in representing the destruction of cells as most advanced at the circumference of the lobules.

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* In one of his cases Riess (*Annalen d. Charité-Krankenhauses*, 1864, Bd. xii. Heft ii. p. 131) measured the liver cells from the yellow portions, and found them on the average to be but .0105 mm. while Henle gives the normal size as ·016. The measurement does not seem to have been made after hardening in chromic acid, but when the cells were quite fresh. Lewitski and Brodowski (*Arch. f. path. Anat.* 1877, Bd. lxx. p. 425) found the cells from the yellow part 3 to 4 times smaller than usual; in the red parts the cells at the periphery of the lobule were swollen (36 μ. to 40 μ.) and rounded.

† Frerichs, *op. cit.* Bd. i. p. 233.

It may not be all at once determined from this rapid examination with the microscope, if the liver suffer a mere fatty infiltration or an acute degeneration. This is often a matter of some trouble. Liebermeister has given rules for settling this question : they are : i. The size of the drops of fat : this may often be very useful, for in fatty infiltration the larger and middle sized fat drops are the commoner, while the smaller and smallest fat drops are seen chiefly in fatty degeneration. If the liver cells be found full of large drops of fat, as a rule there is no need to suspect an acute fatty degeneration: if, however, the liver cells be so filled with small fat drops and granules of fat that the nucleus is no longer visible, then the idea of a fatty degeneration predominates, even if the outline of the cell be sharply defined. ii. The part of the lobule in which the fat-containing cells are found: this is often important, as in fatty infiltration the cells which show this change most are often

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* Foerster, *Handb. d. path. Anat.* Leipzig, 1863, 2te Aufl. p. 179.

† Bamberger, *op. cit.* p. 539.

‡ Handfield Jones, *Lond. Med. Gaz.* 1847, p. 1145.

§ Grainger Stewart, *Edinb. Med. Journal*, 1865, Vol. xi. pp. 323 and 635.

§ Christy Wilson, *ibid.* 1868, Vol. xiii. p. 735.

|| Schultzen und Riess, *Annalen d. Charité-Krankenhauses*, 1869, Bd. xv. p. 87.

¶ Ogston, *British Med. Journal*, 1873, Vol. i. p. 73.

those in the circumference of the lobule, while in degeneration the whole of the lobule suffers. iii. The state of the connective tissue: in cases of degeneration, the connective tissue takes part in the process, and shows granules of fat; but care should be taken to distinguish between drops of fat which merely cling to the connective tissue, but have their source in damaged liver cells; and those which are the result of real fatty degeneration of the connective tissue itself: iv. But the important test of all is to make out that the liver cells have been destroyed; and unless this be done, it must always be doubtful what morbid change has taken place in the liver. Great care must be taken not to press the preparation under the microscope, so as not to break up the liver cells and set the fat drops free. If this care be taken, and yet a large amount of fat be still found in large drops in the cells, the opinion will be given in favour of a fatty infiltration. If, however, after all precautions have been taken, only free drops be seen, either scattered through the field or gathered into groups, and no cells with a clear defined outline and no large drops in the cells, then there can be no doubt that a fatty degeneration is present.[*]

Zenker has paid much attention also to the histology of the two tissues, the red and the yellow patches in the liver. In the yellow, the liver cells are often destroyed, but there yet remain some liver cells which can be recognised as such, in the earlier stage of degeneration; while in red patches, no trace of the liver cells can be found; nothing but a detritus of fine fatty granules with small hæmatoidin crystals.[†]

Most writers agree with Zenker in representing the red patches to be those most advanced in the disease, that no liver cells can be found in the red patches, even when the yellow patches contain cells granular and swollen. Robin and Hiffelsheim, however, found the red patches to contain perfectly normal cells,[*] and Frerichs seems to look upon the reddened part as the earlier stage of the disease, a hyperæmia, while the yellow represents the later.[†]

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[*] Liebermeister, *Beiträge zur path. Anat. u. Klinik d. Leberkrankheiten*, Tübingen, 1864, p. 173.

[†] Zenker, *op. cit.* p. 182.

There is another important histological point on which authorities are deeply divided. It is much disputed if there be an increase of connective tissue, or not, in acute atrophy. Robin, in 1857, seems to have been the first distinctly to affirm that there was an overgrowth of the connective tissue: he speaks of a network of areolar tissue in the midst of the destroyed cells. Further on he speaks of a certain analogy which these cases have with what is seen in cirrhosis, only that in *icterus gravis* the amorphous material is much more abundant, and that the laminated fibres are much less numerous than in cirrhosis. He speaks also of the rapid formation of fusiform bodies and of fibres of connective tissue in the amorphous material.[‡] Virchow also described an overgrowth and thickening of the connective tissue and vessels of the liver in 1863, saying that this showed the existence of a chronic process in the liver.[§]

Altogether about thirteen writers record cases in which the connective tissue in the liver was increased; and these are not limited to the French school, but include observers in Berlin, Vienna, London, Glasgow, Warsaw, and America.[‖] One of the most important of the supporters of Robin's views is Riess. He found, before Zenker, that the connective tissue is most abundant in the red patches and less developed in the yellow. His account is as follows: the connective tissue is developed throughout the whole organ; but in the yellow parts only at the circumference of the lobules, and but little within them: if, however, the process be farther advanced, the connective tissue is very abundant inside the lobules and is less visible about the circumference. In the red patches, the circumference of the lobule shows nothing but connective tissue corpuscles and cell detritus; only a few islets of hepatic cells remaining near the hepatic vein.*

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[*] Hiffelsheim and Robin, *Gaz. méd. de Paris*, 1857, p. 659.

[†] Frerichs, *op. cit.* Bd. i. p. 233.

[‡] Robin, *Mém. lus à la Société de Biologie*, 1857, p. 9. I do not think that Foerster meant to describe any increase of connective tissue: (*Arch. f. path. Anat.* 1857, Bd. xii. p. 361) merely that, after destruction of the cells, the natural network of connective tissue was more apparent.

[§] Virchow, *Monatsschrift f. Geburtskunde*, 1863, Bd. xxi. p. 91.

[‖] I do not know if Merbach intended to describe the overgrowth of connective tissue as visible to the naked eye when he speaks of each lobule in the red patches being surrounded by a grey line. (Schmidt's *Jahrbb.* 1863, p. cxix. p. 38.)

Winiwarter has come to much the same conclusion with more elaborate examinations. He describes the vessels running between the lobules as surrounded by thickly massed lymphoid corpuscles, which also lie between the bundles of connective tissue. These, says Winiwarter, are plainly emigrant white corpuscles and connective tissue corpuscles in proliferation. The blood vessels between the liver cells show an almost complete absence of red corpuscles. Within the vessels, and in the circum-vascular lymph spaces, were many lymphoid elements. The wall of the vessels takes no part in the growth, shown, says Winiwarter, by its freedom from a multiplication of nuclei. These appearances greatly recall those seen in leucæmia. Winiwater likewise gives drawings showing an increase of the connective tissue and abundance of nuclei between the cells. In places where changes have farther advanced, there is abundance of spindle-shaped cells, and finely fibrillated connective tissue, and the vessels between the liver cells can no longer be seen. When the liver cells are fully destroyed, they carry with them the newly-formed tissue so that nothing but a molecular detritus is found. On this overgrowth of the connective tissue Winiwarter founded a distinction between acute atrophy and poisoning by phosphorus; in this latter the cells become simply fatty, filled with large oil drops; there is no increase of connective tissue.* Cornil, on the other hand, finds an increase of the connective tissue in all cases of parenchymatous degeneration, whether the cause be small-pox or puerperal fever.†

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* Riess, *Annalen d. Charité*, 1865, Bd. xii. Heft. ii. p. 122.

Liebermeister may be looked upon as the leader of those who deny that increase in the connective tissue is essential to acute yellow atrophy. He thinks that, in those cases in which the connective tissue has been found more developed than natural, the appearance is due to a growth in the liver foregoing the parenchymatous degeneration. And in most of the cases in which an increase of the connective tissue has been found, Liebermeister inclines to the belief that the increase is only apparent, and that the prominence of the connective tissue is due to the disappearance of the cellular elements of the liver, as Wedl remarks.‡ Liebermeister thinks that Robin's cases may be explained on this hypothesis. Riess and Winiwarter's cases had not been published when Liebermeister wrote, and Liebermeister looks upon the presence of an overgrowth of the connective tissue in the liver as a mere accidental complication.§

I do not think that this view can now be maintained. The cases in which an overgrowth has been found are too many, and the observers too good, for the appearance to be explained by accident, or a false interpretation of objects seen under the microscope. It must be owned that many cases of acute yellow atrophy do show an increase in the connective tissue. Whether this be constant is very doubtful; and I incline myself to the belief that in some there is an increase and in others none. I was unable to detect any increase in a case which I examined some years ago, and it is possible that the difference between observers may arise from the varying length of time which the disease has lasted. Zenker remarks on the hardness and toughness of the red parts of the atrophied liver,[*] and these red parts are generally believed to be the most far advanced portions of the disease.

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* Winiwarter, Stricker's *Med. Jahrbb.* 1872, p. 256.

† Cornil, *Compte rendu des Séances de la Societé de Biologie*, 1875, p. 306.

‡ Wedl, *Grundzüge d. path. Histologie*, Wien, 1854, p. 297.

§ Liebermeister, *op. cit.* p. 180.

The idea that the increase of connective tissue is due to the length of time that the disease has lasted, is somewhat favoured by examining the clinical notes of the cases in which the greatest amount of connective tissue has been seen. In Riess' two cases, the illness began in the one on Sept. 24, and death took place on Nov. 10, jaundice having lasted nearly a month. In the other, the illness began eight weeks before death.[†] In Dr. Moxon's case the jaundice lasted about eight weeks.[‡] In one of Dr. Hilton Fagge's cases the patient had been jaundiced for three months.[§] In Picot's case there is some mistake about dates, as he states that the jaundice began on April 31, a day that does not exist, and that death took place on August 4. The patient was admitted on April 29, for syphilis.[¶] In Dr. Wadham's case the jaundice lasted six weeks.[**] In Fritz' case, jaundice came on in March and death took place on May 13.* In Klob's case the patient was seized with the ordinary appearance of acute yellow atrophy four weeks before death.† In Dr. Coats' case‡ and in one of Dr. Hilton Fagge's cases§ in which the indications of an overgrowth of connective tissue were but slight, the disease had in each lasted about a fortnight. However, in Vallin's case the patient only went to the doctor on October 7, became jaundiced on the 11th, and died on the 14th,‖ and in one of Winiwarter's cases the patient died within 24 hours after the appearance of the jaundice.¶ Robin gives description only of the appearances seen after death, but in a case recorded by himself and Hiffelsheim, the patient seems to have died within a few days of the first symptoms.** I think that this point will deserve further attention at the hands of observers.

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[*] Zenker, *op. cit.* p. 175 note, and p. 185. In Lewitski and Brodowski's account (*Arch. f. path. Anat.* 1877, Bd. lxx. p. 425) of the histology of the red part of the liver, one is reminded of the hypertrophous cirrhosis described by Hanot.

[†] Riess, *loc. cit.*

[‡] Moxon, *Trans. of the Path. Soc. of Lond.* 1872, Vol. xxiii. p. 138.

[§] Hilton Fagge, *ibid.* 1867, Vol. xviii. p. 136.

[¶] Picot, *Journal de l'Anatomie*, 1872, p. 246.

[**] Wadham, *Lancet*, 1872, Vol. i. p. 288.

It has been long known, for it was known to Rokitansky, that cirrhosis may complicate acute atrophy or that patches of acute yellow atrophy may be seen in cirrhotic livers;†† and Frerichs has recorded a case of cirrhosis in which the cells of the liver were everywhere destroyed.‡

Waldeyer has published a very interesting and important case, the heads of which will be given: the liver tough, leather-like in consistence, and of a reddish-yellow colour with a tinge of grey. The tissue round the vessels showed a thick layer of connective tissue. In the midst of the liver tissue were yellow nodules in which the markings of the lobules could still be made out. Also very small points of a black blue colour could be seen scattered through the liver substance.

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* Fritz, *Gaz. d. Hôp.* 1863, p. 81.

† Klob, *Zeitschrift d. kk. Gesellschaft d. Aerzte zu Wien*, 1858, p. 736.

‡ Coats, *Brit. Med. Journal*, 1875, Vol. i. p. 847.

§ Hilton Fagge, *Trans. of the Path. Soc. of Lond.* 1869, Vol. xx. p. 212.

‖ Vallin, *Gaz. hebd.* 1867, t. iv. p. 487.

¶ Winiwarter, *op. cit.* p. 258. Cf. Baader and Winiwarter, *Wien. med. Wochenschrift*, 1870, p. 1404.

** Robin and Hiffelsheim, *Gaz. méd. d. Paris*, 1857, p. 659.

†† Rokitansky, *Hand. d. path. Anat.* Wien, 1842, Bd. iii. p. 339.

‡‡ Frerichs, *op. cit.* Bd. ii. p. 11.

Under the microscope the grey red part consisted solely, excepting the vessels, of young connective tissue, rich in cells, and with small branching tubular bile ducts. In many places this connective tissue locked quite like young granulation tissue, such as is found in the neighbourhood of tumours, especially sarcomata. No normal liver cells could be found; but scattered about or contained in the bile ducts, were rounded angular bodies like cells, filled with yellow-brown pigment, bodies which clearly must be looked upon as the remains of liver cells. These were sometimes arranged so as to form ducts, and were clearly in communication with the small bile ducts spoken of. The larger bile ducts contained an epithelium very cloudy, thick, and irregularly accumulated. Biliary casts, such as Oskar Wyss has described, were found. In other places the capillary bile ducts were seen with well preserved epithelium, and seemed to have shot forth blind processes of ducts, so that a regeneration of the liver tissue seemed about to be taking place from the bile ducts.

The arteries as well as the larger ducts were surrounded by a thick and firm ring of connective tissue. The walls of the hepatic veins were also thickened.

The patient fell ill on November 20th and died on January 6th of the following year, the jaundice having lasted nearly the whole of the time.* An account of the bacteria seen in the liver will be given below.

Winiwarter has seen the same appearances as Waldeyer: he says the bile ducts have many branches, the larger showing a good epithelium which consists of many-sided cells, and are bounded by a structureless *membrana propria*, and show a distinct cavity. The sheaths are of small diameter when seen from the cut surface, consisting simply of a *membrana propria* in the cavity of which lie two or three small rounded cells with large nuclei. In other places these cells become larger, almost cylindrical, and in still more developed parts are seen groups of irregular polygonal cells, much larger than those spoken of before, arranged longitudinally, and surrounded by a structureless sheath, and having a central cavity. These are very like what is seen in the normal liver, and suggest that a regeneration of the liver tissue may be taking place, just as Waldeyer said.[*] These views have been adopted by Klebs,[†] and by Eppinger,[‡] and it is clear that the end of the process in acute atrophy is not reached when the cells are destroyed, as was formerly the belief.

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* Waldeyer, *Arch. f. path. Anat.* 1868, Bd. xliii. p. 533.

It was unlikely, at a time when so much attention has been paid to the germ theory of disease, that acute yellow atrophy should escape the fate of nearly every other disease in the nosology[§] and have no special monad assigned to it. Yet at present Eppinger seems inclined to attribute all the troubles of this disease to a common organism, the *Microsporon septicum*[‖] which he and Klebs have found in great abundance in the bile ducts. Here bacteria and micrococci were found in every stage of developement; also in great abundance in the stomach and intestines, the epithelium of which was almost entirely taken up by these organisms.

The first to notice the presence of bacteria in acute yellow atrophy was Waldeyer. The black blue points which have been already spoken of were found, when looked at carefully, to have a small yellow white point in their centre. The pigment consisted of black crystalline granules which lay in the remains of the cells of the parenchyma. The pigment was rapidly dissolved by hydrochloric acid, and coloured blue by ferrocyanide of potassium. After the action of the acid the yellow grey point came into view, and was found to be made up of colonies of bacteria. The bacteria were only found in the pigmented parts; and the pigment was never found without bacteria. Bacteria and pigment were found likewise in the stomach, pancreas and right suprarenal capsule.[*]

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[*] Winiwarter, Stricker's *Med. Jahrbb.* 1872, p. 263.

[†] Klebs, *Handb. d. path. Anat.* Berlin, 1869, Bd. i. p. 419.

[‡] Eppinger, *Prager Vierteljahrsschrift*, 1875, Jahrg, xxxii. Bd. i. p. 32.

[§] See Klebs' Beiträge zur Kenntniss der pathogenen Schistomyceten in *Arch. f. exp. Path.* Bdd. i. iii. and iv.

[‖] Eppinger, *op. cit.* p. 41. Charcot and Gombault found a considerable quantity of vibriones in the bile ducts of an animal whose common duct had been tied. (*Archives de Phys.* 1876, p. 276.)

Zander has recorded a case in which the examination was made 54 hours after death, and scrapings of the liver substance showed bacteria in active movement.[†] The time that passed between death and the examination is, however, too long for any trust to be put in Zander's observation.

An excellent observer, Dr. Coats, was unable to find any bacteria in his specimen, although carefully looked for.[‡]

It is of importance to note the results of the few chemical examinations of the liver which have been made. Sugar has been found to be absent from the liver in states closely akin to acute yellow atrophy such as poisoning by phosphorus, arsenic, etc. In like manner Frerichs and Städeler,[§] Oppolzer[‖] and Liebermeister[¶] found no sugar in their cases, and it is highly probable that the glycogenetic function of the liver is abolished in all this family of disorders. Pleischl, however, in one case found sugar in the watery extract of the liver.[*]

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[*] Waldeyer, *op. cit.* p. 538.

[†] Zander, *Arch. f. path. Anat.* 1874, Bd. lix. p. 153.

[‡] Coats, *Brit. Med. Journal*, 1875, Vol. i. p. 847.

[§] Frerichs and Städeler, Müller's *Arch. f. Anatomie, &c.* 1854, p. 384, note.

[‖] Oppolzer, Schmidt's *Jahrbb.* 1860, Bd. cvii. p. 34.

[¶] Liebermeister, *op. cit.* p. 239.

Perls, in Rehn's case, estimated the amount of fat present in the liver, and found it, *i.e.* all that was soluble in æther, to be 7·6 *per cent*. In the healthy livers of two grown-up people, the percentage was 2· and 3·4, while in a highly fatty liver of a child of 6 months, the percentage was 19·5.[†]

Frerichs first drew attention to the presence in the liver of certain crystalline bodies, leucin and tyrosin,[‡] and they were made of much importance in the diagnosis of the disease. Scherer found tyrosin, not more than ·098 grm., and leucin, about 1·386 grm. in the liver of one of Bamberger's cases. Hypoxanthin and xanthoglobulin were also found.[§] Folwarczny also found a considerable amount of leucin in the liver of two cases of Standthartner's.[‖] Tyrosin does not seem to have been found. Liebermeister also found leucin and tyrosin in one of his cases.[¶] Sander[**] and Pleischl[††] seem to have found neither leucin nor tyrosin in their cases. Wiedemeister could find no leucin nor tyrosin in the liver of Foerster's case when quite fresh: but after it had been kept 8 days in spirit these bodies were detected.[§§]

In some cases a crystalline efflorescence, which, when looked at under the microscope, has had the appearance of tyrosin and leucin, has been found in the vessels of the liver or on the cut surface after being exposed to the air. It seems scarcely necessary to warn observers against drawing any conclusions from facts observed after this fashion. To render the presence of leucin or tyrosin even probable, it is necessary that a prolonged chemical analysis should be undertaken, and these bodies searched for and estimated in the manner described in the handbooks of physiological chemistry.

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[*] Pleischl, *Wien. med. Wochenschrift*, 1855, p. 21.

[†] Perls, *Berlin. klin. Wochenschrift*, 1875, p. 651.

[‡] Frerichs and Städeler, *op. cit.* p. 382.

[§] Scherer, *Verhandl. d. phys. med. Gesellschaft in Würzburg*, 1858, Bd. viii. p. 283.

[‖] Standthartner, *Zeitschrift d. kk. Gesellschaft d. Aerzte zu Wien*, 1858, p. 787.

[¶] Liebermeister, *op. cit.* p. 188.

[**] Sander, *Deutsche Klinik*, 1860, p. 34.

[††] Pleischl, *loc. cit.*

[§§] Foerster, *Arch. f. path. Anat.* 1857, Bd. xii. p. 363.

It is also of importance to bear in mind that leucin is, according to Radziewsky, a constant constituent of the healthy liver; tyrosin, not. The same observer found leucin to be wanting in the healthy brain, blood, and urine; to be present in the healthy spleen; doubtfully in the kidneys.*

Frerichs seems to look upon these bodies as replacing the urea, the outcome of the deep changes in nutrition which accompany acute atrophy.† It is thought by some that leucin is only a stage in the process which converts albumen into urea. Liebermeister, on the other hand thinks that leucin is an outcome of the decomposition of the liver cells.‡

It seems to me probable that where no chemical examination has been made and simply a crystalline efflorescence examined, that the so-called leucin and tyrosin may be simply the product of decomposition of the liver from putrefaction. The chemical nature of these crystals is, as stated above, most uncertain.

It is stated that leucin and tyrosin have been found in other organs of the body: in the brain, kidneys, spleen, blood, &c.‖

Liebermeister thinks it probable that a decrease or complete arrest of the secretion of bile takes place in acute yellow atrophy. He finds that out of 79 cases, the gall bladder was found empty in 12; and in 24 cases only was the amount of bile natural.*

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* Radziewsky, *Arch. f. path. Anat.* 1866, Bd. xxxvi. p. 1.

† Frerichs, *op. cit.* Bd. i. p. 241.

‡ Liebermeister, *op. cit.* p. 251. Cf. Virchow, *Arch. f. path. Anat.* 1855, Bd. viii. p. 355.

‖ Neukomm (*Arch. f. Anat. Phys.* 1860, p. 1) has found leucin and tyrosin in many organs in many diseases, but the test applied seems in many cases to have been not chemical, but only that given by the microscope.

In the greater number of cases the bile ducts are seen unstained by bile, so that there can be no doubt that there is a great decrease in the quantity of the bile which flows into the duodenum. It must not, however, be too hastily assumed, either from this fact, or from the fact that the gall bladder is often found empty, that the liver has ceased to secrete bile, as the liver might continue to pour into the radicles of ducts bile which could not find its way into the duodenum from obstructions of the ducts lower down in the liver. Still it is probable that with the loss of the power of making glycogen, the power of making bile goes too, and Oppolzer could find no bile acids in the substance of the liver of one of his cases.† Pleischl on the other hand found them.‡ This is a point worthy of attention by future observers.

Frerichs found both bile pigment and bile acids in the bile from the gall bladder of one of his cases.‡ Sander found no bile acids, bile pigment, nor cholestearin in the fluid from the gall bladder of one of his cases.§ Scherer found both of the bile acids, but no tyrosin nor leucin.‖ Huppert found no bile acids.¶

Hünicker, in a somewhat uncertain case of acute yellow atrophy, found the gall ducts, both inside and outside the liver, filled with a dirty yellow croupous exudation: some of those ducts within the liver were dilated into cysts and filled with pus-like material.[*] The liver was not examined with the microscope after death.

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* Liebermeister, *op. cit.* p. 238.

† Oppolzer, *loc. cit.*

‡ Pleischl, *loc. cit.*

‡ Frerichs, *op. cit.* Bd. i. p. 211.

§ Sander, *Deutsche Klinik*, 1860, p. 34.

‖ Scherer, *Verhandlungen der phys.-med. Gesellschaft in Würzburg*, 1858, Bd. viii. p. 283.

¶ Huppert, *Arch. d. Heilkunde*, 1864, p. 255.

Gall stones are not commonly found in acute yellow atrophy. The greater number of the patients are too young for such to be seen in any numbers. Yet Bamberger found two black concretions in a woman aged 20,[†] and Burkart also two gall stones in a woman of the same age.[‡] Frerichs likewise found the bile in the gall bladder of a woman aged 33 to contain small black concretions.[§]

Wunderlich found the mucous lining of the gall bladder swollen, with minute hæmorrhages.[‖]

THE PATHOLOGY OF ACUTE YELLOW ATROPHY.

The cause of the jaundice in acute yellow atrophy is still thought obscure by many. In the earliest recorded cases no obstruction in the larger ducts was found and the jaundice seemed therefore hard of explanation. It is now generally agreed that the stools are free from colour and the ducts free from bile staining, and various methods to account for the jaundice are in vogue. Some of these assume a state of things at variance from that now stated; as that the stools and ducts are coloured, or the ducts coloured and the stools free from colour.

The various explanations may be divided into four heads:

i. Jaundice from suppression of secretion.

ii. Jaundice from paralysis of the larger ducts.

iii. Jaundice from a state of the blood akin to pyæmia &c.

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[*] Hünicker, *Berlin. klin. Wochenschrift*, 1870, p. 326.

[†] Bamberger, *Deutsche Klinik*, 1849, p. 98.

[‡] Burkart, *Ueber acute gelbe Leberatrophie*, Diss. Inaug. Stuttgart, 1872. p. 7.

[§] Frerichs, *op. cit.* Bd. i. p. 211.

[‖] Wunderlich, *Arch. d. Heilkunde*, 1863, Jahrg. iv. p. 148.

iv. Jaundice from some obstruction high up in the liver ducts.

i. The theory of jaundice from suppression of the functions of the liver found great favour with the earlier writers, Alison,[*] Handfield Jones,[†] and Budd,[‡] and, more lately, with Liebermeister, who leans decidedly to this view.[§] The physiological difficulties of the theory of jaundice by suppression have already been discussed, and there is at the present moment no need to add any further remarks.

ii. Theodor von Dusch in 1854 formulated a theory that the jaundice was due to a paralysis of the gall ducts and lymph vessels. Through the paralysis of the gall ducts jaundice was caused without any narrowing of the ducts; for, according to Frey's views,[‖] the gall ducts have a kind of peristaltic movement which pushes on the bile into the bowel; and if the ducts cease to move the bile stagnates. This view seems to be supported by Henoch.[¶]

Ozanam had, some years before, set forth a theory precisely the opposite to that of von Dusch's, a return to the *icterus spasticus* of the older authors. There is a spasmodic constriction throughout the whole of the system of bile ducts, which of course hinders the descent of the bile, and at the same time this constriction disappears within a few hours after death.[**]

iii. Dr. Murchison's reason for believing that the jaundice in acute yellow atrophy is hæmatogenous is apparently based upon his belief that the stools in acute yellow atrophy are coloured by bile, a statement however, to which most observers are opposed. Dr. Murchison thinks that the jaundice is due to a poisoned state of blood.[*] The view of a hæmatogenous jaundice appears to be also accepted by Leyden, although he does not seem really to decide betwixt the varying views in his account of them.[†] The whole question of hæmatogenous jaundice has been discussed in the opening chapter on jaundice and the reasons for its rejection need not be here repeated.

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[*] Alison, *Edinb. Med. and Surg. Journal*, 1835, Vol. xliv. p. 287.

[†] Handfield Jones, *Lond. Med. Gaz.* 1847, new series, Vol. v. p. 1145.

[‡] Budd, *On Diseases of the Liver*, Lond. 1857, 3rd ed. p. 286. Lebert also seems inclined to discuss this hypothesis favourably (*Arch. f. path. Anat.* 1855, Bd. viii. p. 188.)

[§] Liebermeister, *op. cit.* p. 239.

[‖] Th. von Dusch, *Untersuchungen u. Experimente als Beitrag zur Pathogenese des Icterus*, Leipzig, 1854, p. 37.

[¶] Henoch, *Klinik d. Unterleibsk.* Berlin, 1852, Bd. i. p. 291. Cf. p. 277, note.

[**] Ozanam, *De la forme grave de l'ictère essentiel*, Thèse de Paris, 1849, p. 69.

iv. Buhl deserves the credit of having been the first to suggest a really rational interpretation of the phænomenon of jaundice. He thinks it most probable that the beginnings of the bile ducts are filled by a fattily degenerated epithelium, and thus a mechanical cause for the jaundice set up.[‡] It is clear that if the jaundice be due to some mechanical impediment it must be high up in the small ducts, since the larger ducts are patent and uncoloured by bile. Within the last few years Cornil has shown that this hypothesis of Buhl's was quite right. He finds, not merely in cases of *icterus gravis*, but in all cases of parenchymatous degeneration of the liver, that the interlobular gall ducts are filled up with epithelium.[§] Bamberger supports Buhl's views,[‖] and taken together with Cornil's observations, they certainly seem to me the most reasonable of the theories yet set forth as to the cause of the jaundice.

In like manner Frerichs asserts a mechanical cause for the jaundice. There is an exudation in the periphery of the lobules, by which the beginnings of the gall ducts are compressed and the bile formed within the lobule pent up; the bile therefore prefers to pass into the circulation.[*] Frerichs' theory of an exudation, having been revived by Winiwarter and others, in the shape of an overgrowth of the connective tissue of the liver, may also receive due consideration.

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[*] Murchison, *Clinical Lectures on Diseases of the Liver*, London, 1868, pp. 225 and 395. In Dr. Murchison's own case the bile ducts, though patent, showed no tinge of bile: a proof, one would think, that no bile passed down them, although the fæces were yellow.

[†] Leyden, *Beiträge zur Pathologie des Icterus*, Berlin, 1866, p. 170. Cf. p. 11.

[‡] Buhl, *Zeitschrift f. rat. Med.* 1854, Bd. iv. N.F. p. 355.

[§] Cornil, *Compte rendu des Séances de la Société de Biologie*, 1875, p. 306.

[‖] Bamberger, *Khten. d. chyl. Systems*, Erlangen, 1864, p. 539.

Other writers consider that the jaundice is due to a catarrh of the bile ducts, explaining its origin in the same manner that many pathologists do that of simple jaundice. When the ducts are found free from bile, it is supposed that the catarrh has extended up into the finer ducts, which being filled by plugs of mucus hinder the descent of the bile. This view is supported by Oskar Wyss[†] and Ebstein's[‡] experiments, who found in the livers of men or animals poisoned by phosphorus, that the small ducts were plugged by mucus while the large were free. Bright, in one of his cases, remarks that no obstruction was discovered in the ducts which could have prevented the flow of bile from the liver, but some traces of the secretion were found in the smaller biliary ducts.[§] The large ducts do not seem to have been stained with bile; and Bright's cases, therefore, bear a close analogy with those of Wyss and Ebstein spoken of above.

Two theories of the pathology of acute yellow atrophy have prevailed; one which looks upon the disease as a simple disorder of the liver, local at all events in its origin; and another, which looks upon the jaundice and delirium as the expression of a grave general state, akin to the fevers, or the acute specific diseases, typhus and typhoid, and the like. The former prevailed when first the disease began to be studied, but now the second theory is that which has the greater number of adherents; and deservedly so, for the liver is not the only organ found diseased, but changes are present in all the glands and muscles of the body.

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[*] Frerichs, *op. cit.* Bd. i. p. 239.

[†] Oskar Wyss, *Arch. d. Heilkunde*, 1867, p. 469.

[‡] Ebstein, *ibid.* 1867, p. 506 and 1869, p. 379.

[§] Bright, *Guy's Hosp. Reports*, 1836, p. 630, Cf. p. 626.

Richard Bright certainly was the first to call this disease an inflammation of the liver. He says: "In this case there was not the slightest evidence of obstruction to the passage of the bile, nor was there any trace of it in the liver. The bile must have been rapidly absorbed into the system almost at the moment of its formation; and its profuse mixture in the blood seems to have acted as a poison and been the immediate cause of death. I am inclined to consider this as the result of a decidedly inflammatory state of the organ."[*] It would appear to be Bright's opinion that the primary disease is an inflammation of the liver while the general symptoms are due to the jaundice caused by the disease of the liver. This view, of an inflammation of the liver, denied by some,[†] was taken up by the Germans, Wedl,[‡] Bamberger,[§] and Frerichs,[‖] but especially by the followers of Virchow, to whom this notion was particularly welcome, and the disease was described by them as acute parenchymatous hepatitis.[¶] Lately the doctrine of an interstitial inflammation, a cirrhosis, has received much support from the observations made upon the increase of connective tissue within the liver. Robin was the first to find the connective tissue increased,[**] and his observations have been repeated by numerous histologists, English, French, and

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[*] Bright, *Guy's Hosp. Repp.* Vol. i. 1836, p. 626.

[†] Handfield Jones, *loc. cit.*

[‡] Wedl, *Grundzüge der path. Histologie*, Wien, 1854, p. 297.

[§] Bamberger in his first edition adhered to this opinion, but revoked it in his second. (*Vide loc. cit.*)

[‖] Frerichs, *op. cit.* Bd. i. p. 239.

[¶] Foerster, *Handb. d. spec. path. Anat.* Leipzig, 1863, p. 179.

[**] Robin, *Mémoires lus à la Société de Biologie*, 1857, p. 9.

German; so that some, as Picot,[*] look upon acute yellow atrophy as little more than an early cirrhosis. Winiwarter believes that the growth of the connective tissue serves to separate acute yellow atrophy from phosphorus poisoning.[†] It will, however, be seen that several observers have also found an increase of the connective tissue in phosphorus poisoning.

Loeschner has set forth a theory of acute yellow atrophy different from that of all other writers. It is not an inflammation, nor a simple stasis in the portal vessels. It is rather a deep change in the nutrition of the organ. If too little or improper food be taken, absorption goes on ill, the mesenteric glands become swollen and there appears a stasis in the veins of the mesentery, intestine, spleen, and pancreas, in short, of the whole portal system; there is therefore a decreased supply of blood to the liver, and what blood does arrive is diseased; so that the functions of the liver cannot go on: the blood corpuscles are therefore not perfectly destroyed and the bile-making function is injured, so that bile remains behind in the blood.[‡]

It has been mentioned that Theodor von Dusch formulated a theory of nervous disease as the source of acute yellow atrophy.[§] This theory has just been explained, so that it is unnecessary to speak of it again; but an important addition to the preceding theories was made by this author. It has long been known that the bile had the power of dissolving the red blood corpuscles, and von Dusch believed that he had discovered that it had the same influence upon the liver cells. He says that the bile, especially if concentrated, is able make the liver cells transparent and pale, and at last they disappear as a finely granular mass. Here then seemed an excellent explanation of all the phænomena. First a retention of bile from paralysis of the ducts; next, the retained bile, acting upon the liver cells, dissolved and destroyed them. Then, too, in favour of this view was the fact that in the first case in which the liver cells had been found dissolved, and in some others also, there was a permanent tangible obstruction to the flow of bile into the duodenum. But this theory was rudely shaken when Robin[*] and Kühne[†] showed that the liver cells, although rendered transparent and pale by the action of bile, were not dissolved, but could again be brought into view by the action of colouring matters. Dr. H. C. Wood says that the idea of living cells melting away in their own secretion is so opposed to all modern pathology that he wonders at Frerichs stopping seriously to refute it.[‡] Nevertheless Davidson has of late attempted to revive it.[§] This theory can only be admitted possible when some mechanical impediment to the flow of bile exists. In most cases of acute yellow atrophy the ducts are found empty and undilated. To these cases therefore von Dusch's theory cannot apply.

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[*] Picot, *Journal de l'Anatomie*, 1872, p. 256.

[†] Winiwarter, *Medizin. Jahrbb. herausgeg. von d. kk. Gesellschaft d. Aerzte zu Wien*, 1872, p. 269.

[‡] Loeschner, Schmidt's *Jahrbb.* 1856, Bd. xci. p. 205.

[§] Th. von Dusch, *loc. cit.*

It is here necessary to speak of those cases of permanent obstruction to the bile ducts in which after death the liver cells are found dissolved. In my opinion they do not in any way belong to the same category as acute yellow atrophy. It is strange that the first case in which the liver cells were found dissolved was a case of permanent obstruction to the bile duct,* and it is probable on this account that writers, such as Foerster,† have included these cases amongst acute yellow atrophy. Save this solution of the cells, the cases have very little in common with acute yellow atrophy. As a rule they have a long chronic course, towards the end of which the jaundice sometimes greatly decreases, or even disappears. The symptoms are those of the disease which causes the jaundice, and have no likeness whatever to those of acute yellow atrophy, except at the very end, when delirium or coma may appear: none of the reports speak of convulsions. After death dilatation of the ducts is found in all; in one or two the gall stone, the cause of the mischief, had escaped before death into the bowels; in others it remained *in situ;* and in the remainder the disease was caused by cancer of the pancreas or pylorus. In some, and these are those which most closely imitate acute yellow atrophy, there were purulent deposits in the liver; cysts containing pus, formed by the great dilatation of the bile ducts. These cases run a more rapid course than the others and resemble pyæmia in their symptoms. It is these cases which Jaccoud endeavours to bring into the category of acute yellow atrophy under the name of parenchymatous atrophy of the liver. In Jaccoud's own case the liver cells do not seem to have been dissolved, but only infiltrated with fat. Jaccoud divides his cases of parenchymatous atrophy or acholia into three heads: acholia from destructive hepatitis, acholia from steatosis, and acholia from mechanical causes. Acute yellow atrophy, phosphorus poisoning, and chronic obstruction to the ducts may be taken as types.‡

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[*] Robin, *Mém. lus à la Soc. de Biologie pendant l'année* 1857. p. 14.

[†] Kühne, *Arch. f. path. Anat.* 1858, Bd. xiv. p. 324. Genouville (*De l'ictère grave essentiel*, Thèse de Paris, 1859, Canstatt's *Jahresb. f.* 1859, Bd. iii. p. 194) injected a sheep's liver with bile and found after 24 hours that the liver was fully intact.

[‡] H. C. Wood, *American Journal of Med. Sciences*, 1867, Vol. liii. p. 425.

Davidson, *Monatsschrift f. Geburtskunde*, 1867, Bd. xxx. p. 463.

The cause of the solution of the liver cells in these cases seems to me hard of interpretation. At one time I inclined to the belief that the solution might be due to the physiological action of the bile acids which cause a parenchymatous degeneration of the tissues like that caused by phosphorus, arsenic, antimony, alcohol, and other drugs. I do not now think such an opinion tenable, chiefly because I believe the amount of bile acids secreted in jaundice to be too small for such effect. It may be that the change is a necrobiotic one, caused by the pressure of the dilated vessels. Oskar Wyss seems to assert that in these cases the solution of the cells is a simple *post-mortem* phænomenon[*] coming on within 24 hours after death. I fear I cannot agree with him, as I have often kept the livers of patients who have died of obstruction to the ducts, without any preservative fluid, and have found even in the summer that the liver cells still preserved their outline after several days.

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* Thomas Williams, *Guy's Hospital Reports*, 1843, p. 444.

† Foerster, *Arch. f. path. Anat.* 1857, Bd. xii. p. 354.

‡ Jaccoud, *Leçons de Clinique méd.* (Lariboisière) Paris, 1873, p. 537.

Horaczek may lay claim to have been the first to suggest that acute yellow atrophy was a general disorder, forasmuch as he thinks it to be due to some primary change in the blood, some change out of harmony with the nervous system.[†] Though the talk about some change in the blood is not what we look upon now-a-days as a very accurate or scientific statement, yet I suppose in Horaczek's days that it conveyed a definite and suggestive meaning. Notwithstanding this, there can be no doubt that the first to decidedly teach that this disease was a general and not a local one was Buhl. He believed that the state of the liver was only a part of a general disorder, shown also by the swelling of the spleen, the bleeding from the stomach and kidneys, as well as by the decrease of the force of the heart. Acute yellow atrophy is allied on one side with typhoid fever, *typhus icterodes*, or bilious typhoid, and yellow fever; on the other with pyæmia, the bites of vipers, &c.[*] Immediately after, Lebert assented to these propositions, but in a somewhat more doubting fashion.[†] He says that although on one side he feels disposed to the view of a cholæmia, yet the clinical and *post-mortem* appearances seem to point with a greater amount of probability to a general disorder. Wunderlich seems unable to make up his mind if the disease be merely the wide-spread appearance of a local disorder or a general disease like typhoid.[‡] Some of the cases he seems to think allied with malignant small-pox, measles, scarlet-fever, and the like.[§]

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[*] Oskar Wyss, *Arch. f. path. Anat.* 1866, Bd. xxxv. p. 553. Skoda asserts that this is Virchow's opinion; and that, according to Virchow, the solution of the liver cells in acute yellow atrophy is always a *post-mortem* phænomenon. (*Allg. Wien. med. Zeit.* 1858, No. 26, p. 101.)

[†] Horaczek, *Die gallige Dyscrasie*, Wien, 1843, p. 6.

Liebermeister's observations gave a great support to the belief that acute yellow atrophy was a general disease. He pointed out that not merely the liver cells, but the kidney epithelium and the fibres of the heart were constantly in a state of parenchymatous degeneration, and that there was great likeness, if not absolute identity, between this disease and yellow fever and phosphorus poisoning.[‖] Of late writers have seemed almost unanimous in agreeing that the disease is a general one, Bamberger even retracting an opinion which differed from this.[¶] Trousseau compares the disease to a pyrexia,[§] and says that the change in the blood is the first disorder. Leyden thinks the disease a general one, caused by a poison either begotten in the œconomy or brought in from without.[*] Dr. H. C. Wood is confident that it is a fever and that the disease is probably due to the presence of leucin, from which he calls it leucinosis.[†]

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[*] Buhl, *Zeitschrift f. rat. Med.* 1854, N.F. Bd. p. 355.

[†] Lebert, *Arch. f. path. Anat.* 1855, Bd. viii. p. 186.

[‡] Wunderlich, *Arch. d. Heilkunde*, 1860, p. 229.

[§] p. 231.

[‖] Liebermeister, *Beiträge zur path. Anat. u. Klinik d. Leberkrankheiten*, 1864, p. 163.

[¶] Bamberger, *Krankheiten des-chylop. Systems*, Erlangen, 1864. p. 537.

[**] Trousseau, *Clinique méd.* Paris, 1865, t. iii. p. 268.

Some light may be thrown upon the pathology of acute yellow atrophy by a comparison of its phænomena with the diseases which stand with it in the genus *icterus gravis*, and even with other more distantly related disorders. It has been noticed in the chapter which deals with the ætiology of acute yellow atrophy, that some of the first cases recorded happened in families, one member of which might die with symptoms of *icterus gravis*, another fall ill with simple jaundice and soon recover. The same may be noticed not merely in families but in houses, and on a larger scale in the epidemics of jaundice. It seems very probable, from the study of the history of these epidemics, that they are due to some influence which may be conveniently called a poison. The action of this poison is not commonly intense, so that signs of gastric catarrh and of jaundice are, in a great number of cases, the only symptoms. But in some rarer cases, the influence seems to have graver effects, and the patient dies with all the symptoms of an *icterus gravis*, and at least in one case of those amongst kindred, there have been seen, after death, all the morbid appearances of acute yellow atrophy.

Another variety of *icterus gravis*, more allied, it must be owned, in its morbid anatomy than in its symptoms, is the yellow fever. Here there can be no doubt of the jaundice, the nervous symptoms, and the hæmorrhagic diathesis.

After death the likeness is more complete; there is solution or fatty degeneration of the liver cells, the kidneys and heart show changes like those in acute yellow atrophy, there is little or no urea in the urine, and the liver is free from sugar. In this disease there is, it is highly probable, some poison in operation, the effects of which are seen in the dead body.

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[*] Leyden, *Beiträge zur Pathologie des Icterus*, Berlin, 1866, p. 160.

[†] H. C. Wood, *American Journal of Med. Science*, 1867, Vol. liii. p. 418.

But to leave the cases which in all likelihood are due to poison, and to come to those in which a poison is undoubtedly in action. In poisoning by phosphorus there is the closest likeness to, if not identity with, the process of acute yellow atrophy. Some, indeed, assert that all cases of acute yellow atrophy are of necessity cases of phosphorus poisoning; but this is going too far. Then again, poisoning by a large number of substances, arsenic, antimony, and alcohol being among the chief, brings out nearly the same symptoms, and certainly the same morbid appearances after death; so that these universal parenchymatous degenerations, when they can be traced home to their source, in nearly all cases own the action of some poison as the first part of the process.

If, then, a reasoning by analogy hold good in this case, the cause of the parenchymatous degenerations, and therefore of the whole disease, would be some poison, or perhaps it would be safer to say, some influence, generated in the body or brought in from without.

The nature of this is quite unknown. The bacteria noted by some observers seem to be by no means a constant appearance, and cannot therefore be admitted as an essential part of the phænomena of acute yellow atrophy. It is mere speculation to look upon it as malaria or miasm, or some species of infection. It cannot be thought, as Spiegelberg seems to suggest, that it is the bile acids circulating in the blood from the jaundice;[*] for there can be no doubt, from a consideration of the clinical history of the disease, that the jaundice is a sequence of the poison, not the poison of the jaundice. The bile acids, it is known from the researches of Leyden,[†] do cause a parenchymatous degeneration of all organs when injected under the skin.

It will at once be objected to the theory of poisoning that the beginnings of parenchymatous degeneration so commonly seen in febrile diseases are due, not to a poison, but to the increase in the body-heat; and that if this be so in the large number of cases which are due to pyrexia, why should not some other influence than poison be at work in acute yellow atrophy? This is a very pertinent objection, and should be well weighed. For it must be remembered also that in pregnancy a like state is set up, and it is not yet proved that the parenchymatous degenerations of pregnancy are due to a poison, though, as Dr. Barnes has pointed out,[‡] the state of pregnancy offers many analogies to that of poisoning.

The temptation to look upon acute yellow atrophy as identical with phosphorus poisoning is certainly very great. The features of the two states bear the closest resemblance. Both are seen much more often in women than in men, and preserve much the same proportion; both are rare in childhood, common from puberty to about 35, and then again become rare. The symptoms likewise are almost identical; a gastric catarrh followed by jaundice, during the course of which nervous symptoms and hæmorrhages are seen, the end being in most cases fatal. The only clinical distinction which has been made, and in my opinion not very successfully, lies in the state of the urine. Schultzen and Riess, as already stated, believe that in acute yellow atrophy leucin and tyrosin are present in the urine; while in phosphorus poisoning these bodies are absent.[*] Setting aside the cases of phosphorus poisoning in which these bodies are said to have been found, but which show some uncertainty, I must own that I do not think the distinction will hold. It seems very improbable that if the same grave changes in nutrition take place in both states, such bodies as leucin and tyrosin should not be common to both. The morbid anatomy of both diseases has, however, been warmly contested. The state of the kidneys, stomach, glands, and muscles is admitted to be identical in both: but the liver is said by some to be always enlarged in phosphorus poisoning, and to show no real fatty degeneration, but a mere fatty infiltration. This again is denied to be true constantly. It is said, with a good show of reason, that the size of the liver in both diseases depends upon the length of time that the disease has lasted; that the liver is large if the disease end early, and small if the disease last long in both. As to the histological characters of the liver: Schultzen and Riess,[†] and Winiwarter,[‡] seem inclined to attach much importance to the increase of connective tissue which they find in some cases of acute yellow atrophy, and which they believe to be peculiar to it. The same, however, has been found in cases of phosphorus poisoning[§] if the disease only last long enough, a common end of many cases of parenchymatous degeneration of the liver.

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[*] Spiegelberg, *Lehrb. d. Geburtshülfe*, Lahr, 1877-78. Gerhardt thinks that in many cases the poison arises from the putrefaction of the dead *fœtus in utero*. (*Ueber Icterus gastro-duodenalis*, in Volkmann's *Sammlung klin. Vorträge*, Leipzig, 1870-75, p. 107.)

[†] Leyden, *Beiträge zur Pathologie des Icterus*, Berlin, 1866, p. 57.

[‡] Robert Barnes, *Brit. Med. Journ.* 1877, Vol. ii. p. 209.

It is further urged that the processes in acute yellow atrophy and in phosphorus poisoning are altogether unlike; that in the former, the cells do not fill with large drops of fat, but with small-sized granules, some soluble in acetic acid, the others not; and that later on the cells are dissolved into a granular detritus, and that nothing is seen under the microscope but granules and fat; that in the latter the cells are simply filled with fat and suffer no destruction or dissolution.

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[*] Schultzen and Riess, *Annalen d. Charité-Krankenhauses*, 1869, Bd. xv. p. 91.

[†] Schultzen and Riess, *ibid.* pp. 47 and 89.

[‡] Winiwarter, Stricker's *Med. Jahrbb.* 1872, p. 269.

[§] For authorities see section on the Morbid Anatomy of Phosphorus Poisoning.

This is doubtless true of a great number of cases; but it may be disputed if it be universally true, for Oskar Wyss asserts that he has seen the cells of the liver destroyed in cases of poisoning by phosphorus; and some pathologists seem inclined no longer to make the same sharp distinction as formerly between fatty infiltration and fatty metamorphosis. Still even if all these statements be true, it remains that in the majority of cases there is a difference in the appearances seen in phosphorus poisoning, and in acute yellow atrophy, and this would seem to be some evidence that the two diseases are not identical although they be allied. In reply it may be said that cases of acute yellow atrophy are nothing but anomalous cases of phosphorus poisoning, in which the appearances usually seen have varied a little from what is common, as may be seen in nearly all diseases.

It seems to me a very narrow view to look upon all cases of idiopathic universal parenchymatous degeneration as certainly due to only one cause. "Nature," says the old dictum, "is chary of her causes, but prodigal of her results;" but in this matter the reverse is seen, for she is prodigal of her causes, but chary of her results. One result seems to follow a multitude of causes. It would seem as true to assert that alcohol is always the cause of acute yellow atrophy as to assert that phosphorus is; for alcohol causes the appearance of an *icterus gravis* more like if possible to acute yellow atrophy than phosphorus poisoning. It might be asserted, on like grounds, that all attacks of cholera are nothing but poisoning by arsenic, since the morbid appearances seen after death are identical, even down to the very organisms described by Klob as characteristic of cholera.*

There yet remains to be discussed a class of cases, small in number yet very important in their bearing upon the pathology of the disorder. They are those in which the symptoms have been those of *icterus gravis*, yet after death no changes have been made out either with the naked eye or with the microscope; and if competent histologists can find no changes in the liver in such cases, then a heavy blow is dealt at the foregoing notions of the nature of the disorder. The earlier cases, such as those of Valsalva, and even later ones in which the naked eye was the only judge of the freedom of the liver from disease, may be set aside, and this will at once put a good number of cases out of consideration. There then remain a few observations made by careful and competent writers in which there is said to have been no disease discovered with the microscope. As a rule however this means that the cells were found not to be dissolved; so it must not be too hastily inferred that the cells were perfectly natural as regards contents and the like. Such a case is that of Dr. E. L. Ormerod's. A boy aged 13 died in St. Bartholomew's Hospital under the care of Sir George Burrows with well marked symptoms of *icterus gravis*; and after death the liver showed the naked eye appearances of acute yellow atrophy. Sir James Paget found that the liver cells were 'singularly distinct' under the microscope.† But all the evidence that there is in this case, is that the liver cells were not destroyed; but it is not essential to parenchymatous degeneration that the cells should be destroyed; they may merely hold fine granules or fat drops. A like remark may be made upon one of Monneret's cases[*] in which Robin found the "granulations" of the liver to be made up of fat-containing cells, so that they recalled the appearance seen in yellow fever.

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* Virchow, *Arch. f. path. Anat.* 1869, Bd. xlvii. p. 524.

† E. L. Ormerod, *Lancet*, 1846, Vol. ii. p. 5.

Bazin also simply states that the liver cells did not offer the characters described by authors as appertaining to *icterus gravis*, and it may be remarked that the colour of the liver to the naked eye was a deep red.[†] Blachez shortly remarks that the cells in one of his cases preserved their integrity, while in another they were misshapen and full of fat globules.[‡]

Vallin's case must be also reckoned with these; for although he says that the liver cells were everywhere perfectly preserved, yet he adds a very suspicious statement, to wit, that they were slightly pigmented, and in some places held fat. The appearance of the early stage of parenchymatous degeneration might readily be mistaken for a darkening of the cell; the kidney epithelium, in this case, was fatty, but the heart and muscles of the limbs were free from change.[§]

Leaving the cases in which it is merely said that the cells were preserved, there remains a small residuum in which it is asserted that the cells of the liver were perfectly natural when seen under the microscope. Such a case is that of Feltz;[‖] but I must own that the impression left on my mind after reading the account of the symptoms is not that of acute yellow atrophy, but rather of a *delirium tremens* complicated with jaundice. There remain then certain cases examined by Robin, and one reported by Liebermeister, in which there were no changes discovered by the microscope. Robin's evidence on a matter of this kind could be accepted without hesitation; and it is most unfortunate that on this point his report has not been preserved; it is only said that Robin found no appreciable lesion with the microscope,[*] or that the cells were preserved and the tissue was quite healthy.[†] I think it is not unreasonable, in a matter of this character, to ask for evidence at first hand, not passed through the hands of a clinical physician who was only too ready to disparage the use of the microscope and the importance of morbid anatomy. The same objection may be made to Liebermeister's case; it did not come within his own notice, but was seen and reported upon by Greiss, one of the assistant officers of S. Catherine's Hospital at Stuttgart.[‡]

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[*] Monneret, *de l'ictère hém. ess.* Paris, 1859, p. 11.

[†] Bazin, *Gaz. d. hôp.* 1862, p. 489.

[‡] Blachez, *ibid.* p. 193.

[§] Vallin, *Gaz. hebd. de méd. et de chirurgie*, 1867, p. 490.

[‖] Feltz, *Traité clinique et expérimental des embolies capillaires*, Paris, 1870, 2e éd. p. 93

It will be seen that, in my judgement at least, not a single case of *icterus gravis* has yet been published in which there remains no doubt that the liver tissue was free from any change; in no case is it expressly stated that the cells were free from cloudy swelling, a change too frequently overlooked even by careful observers.

The earlier Irish observers, as Marsh,[§] Cheyne,[||] and Griffin[¶] noticing that this disease sometimes followed upon great emotion, and that nervous symptoms were prominent without any special lesion being found after death, thought *icterus gravis* might be a purely nervous disorder. The same idea on the same grounds seems to have been taken up by Dr. E. L. Ormerod.[*] But the spread of the theory that *icterus gravis* is a nervous disorder is chiefly due to Charles Ozanam. His teaching found many adherents across the Channel, the French loving to build great theories on unsafe foundations. They tell us that the doctrine of the association of *icterus gravis* with acute yellow atrophy is but little tasted in France,[†] and that the absence of all change in the liver in so many cases justifies this disbelief.

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[*] Monneret, *de l'ictère hêmorrhagique essentiel*, Paris, 1859, p. 9. At p. 5 is noted a case with naked eye changes, but none with the microscope. It should be noted that Monneret in 1859 still speaks of the "two substances" in the liver.

[†] Hérard, *Union méd.* 1859, t. i. p. 419.

[‡] Liebermeister, *Beiträge zur path. Anat. und Klinik d. Leberkrankheiten*, Tübingen, 1864, p. 369.

[§] Marsh, *Dublin Hospital Reports*, 1822, Vol. iii. p. 276.

[||] Cheyne, *ibid.* 1818, Vol. i. p. 273.

[¶] Griffin, *Lond. Med. Gaz.* 1834, Vol. xiii. p. 801. The brain is the organ primarily at fault.

Liebermeister, although unwilling to acknowledge that any case of *icterus gravis* without change in the liver has yet been made known, yet thinks that even if such a case should be made out there would be no cause for giving up the doctrine that *icterus gravis* is due to changes in the liver. For example, he says, if all blood supply were suddenly cut off from the liver, its function would then certainly be brought to an end, and yet no anatomical change in the cells would be made out. It is well known that the functions of certain glands are greatly influenced by nervous disturbances, so that it is probable the functions of the liver may also be acted on by the nervous system, a direct example of which is seen in the appearance of sugar in the urine after puncture of the fourth ventricle. There is a common belief, amongst physicians and the public, that the emotions greatly influence the functions of the liver, and Liebermeister is of opinion that mental disturbance plays a great part in the ætiology of *icterus*

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[*] E. L. Ormerod, *Lancet*, 1846, Vol. ii. p. 5. Even so recent a writer as Dr. Barnes (*Brit. Med. Journal*, 1877, Vol. ii. p. 211) seems to think that acute yellow atrophy is a disorder of the nervous system.

[†] Reulet, *de l'ictère typhoide*, Thèse de Paris, 1857, p. 24.

gravis. Out of the cases collected it is not stated whether 177 or 86 in number, he found that in 25 some great mental emotion had preceded the disorder, either sudden or long continued.* In my own cases as I have already said, I found only 16 in the 100, and these were not uncomplicated cases. Moreover in all these cases there was found distinct evidence of destruction of the liver cells. Liebermeister thinks that the depressing emotions may be counted in the ætiology of *icterus gravis* in the same rank as poisons and the like. I am myself disposed to think but little of the importance of nervous influences either in the pathology or the ætiology of acute yellow atrophy.

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* Liebermeister, *op. cit.* p. 371, Cf. pp. 222 and 223.

CHAPTER XXII.

THE DIAGNOSIS, PROGNOSIS, AND TREATMENT OF ACUTE YELLOW ATROPHY.

Diagnosis. The diagnosis of acute yellow atrophy is beset with difficulties. In the early stage, before the grave symptoms have appeared, it is simply impossible. Later on, the diagnosis of *icterus gravis* can indeed sometimes be made; but the diagnosis of acute yellow atrophy must, in my judgement, always remain doubtful.

There are many diseases and states which when complicated by jaundice need great experience and judgement to distinguish them from *icterus gravis.* The difficulties of the case become increased twenty-fold when, as in so many of the published cases, there is no trustworthy history. Some of the more prominent diseases will now be spoken of, which, when complicated with jaundice, may be mistaken for *icterus gravis.* In considering all these it is important to keep in mind the succession of events; that in acute yellow atrophy the jaundice usually comes on first and lasts for some time without attracting much attention; and that the nervous symptoms appear later. On the other hand in some of these diseases, the jaundice appears in the midst of the disorder, when a grave character has already been fixed upon the case.

To speak of these cases, more in detail:

i. Many diseases of or injuries to the head. Injuries may, of course, be sometimes excluded: Hæmorrhages into the brain, and meningitis, I do not remember to have ever seen complicated with jaundice. The history would here be of very considerable value. But if a patient suffering from a simple jaundice were to be seized with a ventricular or meningeal hæmorrhage, or a meningitis, the diagnosis would become of great difficulty. Here the absence of bleedings might become of importance. The age of the patient might also be something, but not very much.

ii. Vegetable poisoning, such as opium, belladonna, and the like. Drunkenness is by itself able to cause a state of *icterus gravis*, so that alcohol deserves to be reckoned amongst poisons such as phosphorus, arsenic, and the like. A case of acute yellow atrophy has already been mistaken for belladonna poisoning,* and there seems no reason why the converse should not take place. Here the history again becomes all important.

iii. Pneumonia is sometimes accompanied by jaundice and delirium; the diagnosis ought to be easy in the presence of the signs of lung disease.

iv. Pyæmia is often associated with a slight degree of jaundice. The rigors, rise of temperature, and the presence of a source of pyæmia, ought to enable the diagnosis to be made. The likelihood of multiple abscesses in the liver or a suppurative pylephlebitis ought always to be borne in mind. The fever, and the presence of shoulder-tip pain may help the observer.

v. The fevers, typhoid and typhus, may often give much trouble in diagnosis. Delirium sets in early in typhus, and petechiæ are abundant. There is, however, no vomiting of blood, so constant in *icterus gravis*. The same may be said of typhoid fever; epistaxis is tolerably common in this disorder, but hæmatemesis is rare. And in typhoid, the rose rash and the bronchial complications ought to lead the observer aright. The temperature, also, would be of material help.

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* In one of Dr. Hilton Fagge's cases, the surgeon in attendance thought the delirium due to belladonna poisoning. (*Trans. of the Path. Soc. of London*, 1869, Vol. xx. p. 212.)

vi. Uræmia. In this case the presenc
of albumen in the urine might help to
but in some rare cases of *icterus gravis*,
been found to be highly albuminous. T
not be reminded that some pathologists
he nervous symptoms to be due to uræm

In most of the foregoing states, the di
certain during life, can usually be ma
when the body is opened; if not by gr
changes, such as would be met with i
into the brain, pneumonia, suppurative p
typhoid, yet when the glands are tested
scope, by the absence of parenchymatou
in cases of poisoning by belladonna, o
like.

vii. In the northern parts of Europe, t
any need for a diagnosis to be made
yellow atrophy and yellow fever; this
different in its clinical phænomena fro
atrophy: it occurs in epidemics and o
the Atlantic only. Nevertheless some
yellow atrophy have been called sporadi

viii. From poisoning by phosphorus,
mony, and alcohol, there is, in the a
trustworthy history, no sure means of
ing life.

Frerichs seems to think that the decr
of the liver to percussion is an importa
diagnosis of acute yellow atrophy.† I fe
to share this opinion. My own experien
perience of others, teach me that the liv
imperceptible to percussion even if of nat
state of the urine is also believed by Fre

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* Siphnaios, *Essai sur la fièvre jaune sporadique*, Thèse
Gaz. d. hôp. 1845, p. 369.

† Frerichs, *op. cit.* Bd. i. p. 246.

portant. The appearance of leucin and tyrosin is thought to be of equal value with the decrease in size of the liver. In this belief Frerichs is supported by Schultzen and Riess. These observers hold that leucin and tyrosin are always present in the urine of acute yellow atrophy. In their opinion, they are as characteristic of acute yellow atrophy, as albumen of Bright's disease, or sugar of diabetes. Moreover, their presence in the urine is a means of distinguishing acute yellow atrophy from phosphorus poisoning.[*] This last opinion seems very doubtful, as it would be strange if acute yellow atrophy should alone of all the parenchymatous degenerations be chosen to show this appearance in the urine. Further, certain statements made by these authors themselves throw some doubt upon the universal truth of their belief.[†] They found tyrosin in the blood of dogs poisoned with phosphorus;[‡] Lebert and Wyss found leucin in the blood of a dog and also in man and once in a dog;[§] and these observations are supported by Tüngel[||] and Kohts,[¶] solely it must be owned, on reasons afforded by the microscope. Schultzen and Riess, by the side of sarcolactic acid, note the presence of oxyphenylglycollic acid which they believe to be present in the urine of acute yellow atrophy, and not in that of phosphorus poisoning.

After death, the question of arsenic or antimony poisoning may be settled by the finding of these bodies in the viscera; but with phosphorus and alcohol the case is different, as by the time that death has taken place these bodies can be no longer found. The discussion of the differences found anatomically after death from phosphorus or acute yellow atrophy has been already given (p. 531.)

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[*] Schultzen and Riess, *Annalen d. Charité-Krankenhauses*, 1869, Bd. xv. p. 91.

[†] Schultzen and Riess, *op. cit.* p. 96.

[‡] *Op. cit.* pp. 198 and 110.

[§] Lebert and Wyss, *Arch. gén. de Méd.* 1868, Vol. ii. pp. 269 and 279.

[||] Tüngel, *Klinische Mittheilungen*, 1861, Hamburg, 1863, pp. 134 and 139.

[¶] Kohts, *Deutsches Arch. f. klin. Med.* 1869, Bd. v. p. 185.

When to the acute jaundice there are added the grave symptoms, coma, delirium, or convulsions, and hæmorrhages, especially from the gastro-intestinal tract, then the diagnosis of *icterus gravis* may be made. The decrease in the liver dulness, and the finding of leucin and tyrosin in the urine, add, in my belief, very little to the possibility of a further diagnosis. Good grounds for an opinion, in the absence of all history as to the cause of the *icterus gravis*, seem to me wholly wanting. The matter may, however, be made more easy by the confession of the patient of having taken some noxious drink; or from traces of the poison being found about him. But if, as is the rule with phosphorus poisoning, the patient first come under notice when the grave symptoms have been established, and no history can be had, then I must freely own that I see no certain grounds for forming an opinion on the case.

Prognosis. If, during the course of a simple jaundice such nervous symptoms as delirium and coma appear, the prognosis at once becomes most unfavourable, almost fatal. But it is not absolutely fatal. Recovery has been known to take place after coma and delirium, and severe hæmorrhages have set in, and have lasted for two or three days, and even longer. This seems to be influenced by no age or sex, children of 12 recovering[*] as well as men of 40.[†] Pregnant women have aborted, shown signs of *icterus gravis*, and yet got well.[‡]

Even if the patient recover from the first attack, there seems a possibility of its return; for Dr. Hilton Fagge[§] speaks of a case in which the patient had

[*] Bouchut, *Gaz. des hôp.* 1862, p. 185.

[†] Lavallée, *Bulletin gén. de thér.* 1875, t. lxxxix. p. 462.

[‡] Macnaughton Jones, *British Med. Journal*, 1872, Vol. i. p. 468.
Noblet, *Gaz. des hôp.* 1871, p. 594.

[§] Hilton Fagge, *Guy's Hospital Reports*, 1875, p. 160.

jaundice, hæmatemesis, and delirium, so that his life was despaired of, yet recovered. Within two months he fell ill with like symptoms, and died. After death the liver cells were found dissolved. Leichtenstern, in a very interesting and well-reported case, noticed two separate attacks of grave symptoms, one coming on within a few days after the other; yet the patient left the hospital; with, however, a small liver and a big spleen.[*]

In one or two of the cases of recovery, it is stated that the urea has not been absent; 20 grammes being passed in the 24 hours in Gayda's case.[†]

In some of the cases parotid buboes[‡] and roseolous rashes have been noted:[§] an increase also of the white corpuscles of the blood[‖] has been spoken of.

Treatment. In the early stage of the disease it is impossible to diagnosticate it, and the treatment is that of simple jaundice. When the grave symptoms come on, treatment is too often fruitless. There is no remedy known that will restore the disordered cells to their natural state. The treatment is wholly empirical, and a notice of those means which were employed in the cases of supposed recovery will be the best manner of directing the practitioner in his great perplexity. In some no treatment seems to have been adopted. In others emetics have been used, ipecacuanha for instance;[¶] but the remedy which is most praised by authorities such as Budd[**] and Frerichs,[††] and which

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[*] Leichtenstern, *Zeitschrift f. rat. Med.* 1869, iii. Reihe, Bd. xxxvi. p. 241.

[†] Gayda, *Quelques reflexions sur l'ictère grave*, Thèse de Strasbourg, 1867, reported in Virchow and Hirsch's *Jahresb. f.* 1868, Bd. ii. p. 141. See also Schnitzler, *Deutsche Klinik*, 1850, Bd. xi. p. 286.

[‡] Baudon, *Bulletin gén. de thér.* 1847, t. xxxiii. p. 299. Wunderlich, *Arch. d. Heilk.* 1860, Jahrg. i. p. 31.

[§] Leichtenstern, *loc. cit.*

[‖] Bouchut, *loc. cit.*

[¶] Corrigan, *Dublin. Hosp. Gaz.* 1845, p. 70. Lavallée, *Bulletin gèn. de thérap.* 1875, t. lxxxix. p. 462.

[**] Budd, *On Diseases of the Liver*, London, 1857, p. 288.

[††] Frerichs, *op. cit.* Bd. i. p. 247.

has been employed in the greater numbe
of recovery, is purging. I have myself
from active purging in a grave case o
coma. A boy of 10 had an attack of si
and during the progress of this disor
drowsy, hard to awaken, and slightly
this the percussion dulness of the live
size markedly. Active purging brough
with relief to the head symptoms. The
recovered of his jaundice.

After the dose of purgative have been
advises the use of mineral acids;[*] Bud
in some cases prefers to give nitro-muriat
in the hands of other observers, quinine h
at all events the patients recovered.

In the midst of a sort of epidemic of ja
Ozanam saw advantage from giving 10
ture of aconite to a woman whose s
somewhat alarming, but in whom th
icterus gravis could hardly be made: th
afterwards a benign course. He also sa
cured a case of *icterus gravis* with aconite
of camphor twice daily were given to
patient after two doses of calomel of 10
both of the attacks.[§] Oil of turpentine
of blood have been recommended in pho
ing; and if these means should hold thei
in phosphorus poisoning, it might be as
effect in all the *icteri graves*.

Were I to be so unfortunate as to be
attend a case judged to be acute yellow
liver, I should first administer a smart m

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[*] Frerichs, *loc. cit.*

[†] Budd, *loc. cit.*

[‡] Charles Ozanam, *De la forme grave de l'ictère essentiel,*
p. 99.

[§] Leichtenstern, *loc. cit.*

followed by sulphate of magnesia or soda. Then I should give quinine in large doses, with an admixture of the mineral acids; locally, a large warm linseed poultice over the epigastric and right hypochondriac regions. Leeches over the liver cannot be recommended, still less a general blood-letting. Local hæmorrhages, as epistaxis and hæmatemesis, may be treated by local applications. But so late in the disease it is to be feared that all efforts will prove unavailing, and that the time at which the disease might have been hindered seizing on the patient has passed, never to come back.

CHAPTER XXIII.

YELLOW FEVER: "BILIOUS TYPHOID."

The claim of yellow fever to be admitted amongst the kinds of *icterus gravis* can now no longer be disputed. Whether the appearances seen during life or after death be regarded, the inference must be drawn in the same direction.

Yellow fever usually begins very suddenly, or with very slight *prodroma*, and the outset is accompanied with a remarkable high temperature and frequent pulse. The thermometer at night will read as high as 105° or 106°, and this rise of temperature is accompanied by all the symptoms which usually attend the febrile state. The pulse ranges from 100 to 120, is full and hard. The appetite is lost, there is often vomiting and great thirst, with tenderness or pain in the epigastrium. The bowels are usually costive, and in some cases the stools have already begun to be pale. The skin is hot, dry, and of a peculiar redness; the conjunctivæ injected, the eyes bright; there are headache and backache. The backache is often one of the first symptoms and comes on with extreme suddenness, so that it has given one of the names to the disease, *coup de barre*.

These symptoms of the invasion last from 2 to 4 days; and then the temperature falls, the pulse becomes slow, even if no jaundice come on, and the patient feels much better. In mild cases the improvement is permanent, but in severe cases, the amendment is but for a time, and ushers in the second stage of the disorder, that which gives it a right to be considered an *icterus gravis*.

With the disappearance of the redness, there comes a yellowish tinge of the skin and conjunctiva, the yellow hue to which the disease owes its name. This yellowness, notwithstanding the denial of Trousseau,* is a true jaundice. On this point all recent observers are agreed. The urine likewise contains bile pigment, although the stools, sometimes completely colourless, for the most part are coloured by bile. The serum of the blood and from blisters is intensely yellow. In severe cases the jaundice makes its appearance earlier, about the second day, and it is said by Sullivan to be then a mortal sign; and the same observer remarks that the jaundice may be mild in fatal, and intense in mild, cases.†

With the appearance of the jaundice the temperature and pulse both fall, even below the natural standard. The slow pulse is not, however, solely dependent upon the jaundice, as it appears in cases in which no jaundice is seen. It is noteworthy that some cases die before any jaundice declares itself, although it is, according to Sullivan, certain to be found if looked for after death.‡ The jaundice, as a rule, is quite pronounced on the 4th to 5th day of the disease when the *vomito negro* also begins.

With the disappearance of the fever the epigastric pain and tenderness increase; the vomiting continues, and on the 4th or 5th day of the disease altered blood is brought up. This is the *vomito negro*, and is an almost mortal symptom. With the setting in of bleeding into the stomach, multiple hæmorrhages in other parts make their appearance. Blood is passed by stool, from the nose, gums, mouth, and vagina, and more rarely, in the urine. Petechiæ and ecchymoses are seen under the skin. In short, a severe hæmor-

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* Trousseau, *Clinique méd. de l'Hôtel-Dieu*, Paris, 1865, 2e éd. t. iii. p. 289.

† Sullivan, *Med. Times and Gaz.* 1871, Vol. i. p. 305.

‡ Sullivan, *loc. cit.*

rhagic diathesis is established. In so
blood has also escaped from the uninj
from the eye and ear.

Nervous symptoms of more or less
towards the close of the disorder. La
think that they are no essential part c
yet it cannot be denied that the greater
who have been witnesses of its prog
undoubted changes in the mental state
and wakefulness are very common t
progress of the disorder. In slight ca
be a mere confusion or a slight wand
But in others, and these are the severe a
the delirium is marked, hallucination pe
patients fall into a semi-comatose stat
coma, and violent convulsions may ap
the scene.

The urine in the early stages of the
little unnatural; afterwards it is almos
minous, and in some cases the album
abundant that the urine has become soli
The amount of urea is stated by Chas
been much diminshed in three cases in v
was obtained after death. The analyses
Vardon. In the first case the urea was
the second ·08 grm. in 15 grammes, in
traces could be found, although the urin
man in the early stage of the disease cor
cent. of urea, and some uric acid. In all
uric acid was altogether wanting. The
analysed the blood in the two first cases
says, an increase of urea.† No trust
has, it must again be repeated, yet been
estimating the amount of urea in the blo

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[*] Laroche, *Yellow Fever*, Philadelphia, 1855, Vol. i. p. 37

[†] Chassaniol, *Comptes rendus des Séances de l'Académ*
t. xxxvii. p. 907.

After a patient has died from yellow fever the following appearances are found in the body: there is always jaundice, sometimes slight and only noticed after death. There are numerous petechiæ and ecchymoses, and these are seen also under the mucous and serous membranes. Sometimes hæmorrhages are found between the muscles and into the meninges of the brain. The brain and spinal chord show no changes; neither do the lungs, except in some rare cases, in which hæmorrhagic pleurisy or hæmoptoic infarcts may be present.

In the heart serious changes have been met with. Setting aside the hæmorrhages into the pericardium and endocardium, Riddell has described a parenchymatous degeneration of the fibres of the heart in 30 cases of yellow fever. In most, all traces of striation were gone, and had given way to a granular state. "The molecular change is either complete or well-marked; rarely it is slight or imperceptible"* The same changes have been described by Schmidtlein.† Many authors, without using the microscope, have spoken of the soft and friable state of the muscular walls. According to Riddell, the voluntary muscles do not share in the degeneration.

The stomach contains altered blood, the source of the *vomito negro;* the mucous membrane of the stomach and intestines shows a state of acute catarrh and many ecchymoses.

The spleen is not often found changed; a shrinking of the organ is more common than an increase in size.

The kidneys are found in a state of acute Bright's disease, or cloudy swelling. The cortex is found indistinct in striation.

But it is to the liver that the greatest attention has been paid, since Louis described its yellow appearance as the most constant and important change found in yellow fever.[*] Earlier writers had indeed spoken of this appearance, but had not given it its due weight. All observers since the time of Louis have agreed in speaking of the great change in the character of the liver in yellow fever. Lyons says it is the most remarkable, the most constant, and the most inexplicable, of all the states presented in the *post-mortem* examination. He believes it to be due to a fatty infiltration of the liver.[†] In like manner Alvarenga, who watched the epidemic at Lisbon in 1857 with Lyons, found the liver cells filled with fat so that the nuclei could not be distinguished[‡] and Dutroulau says he found a manifest fatty state of the liver in yellow fever.[§] But the merit of the first demonstration of the real character of this fatty change undoubtedly belongs to the American observations. Dr. Alonzo Clark first drew attention to the fatty state of the liver cells, and asked if the process in the liver might not be called an acute fatty degeneration.[‖] His statements were soon confirmed by Bache who examined a large number of livers and described the liver cells as pale, ill-defined in outline, and less granular; no nucleus could be made out, but one large single oil drop filled the cell, and took the place of the nucleus: the appearance of the preparations suggested the idea that the cells were broken down. Bache agrees with Clark in calling the process an acute fatty degeneration.*

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* J. L. Riddell, *Microscopical Observations pertaining to Yellow Fever*, privately printed, New Orleans, 1854. Quoted by Laroche, *op. cit.* vol. i. p. 393.

† Schmidtlein, *Deutsches Arch. f. klin. Med.* 1868. Bd. iv. p. 84.

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[*] Louis, *Mém. de la Société méd. de Paris*, 1844, t. ii. p. 99. A hundred years before Louis, John McColme noticed the change in the Liver: "In all the cases the liver was changed in part (and sometimes almost the whole) to be more pale, and hard, than natural." John McColme is said to be a man of veracity and observation, who served as regimental surgeon in the West Indies, in the year 1741 and 1742. See Dr. John Hunter's *Observations on the diseases of the army in Jamaica*, Lond. 1796, 2nd ed. pp. 159 and 160. This writer, Dr. John Hunter, is not to be confounded with the great Surgeon, John Hunter.

[†] Lyons, *Report on the Pathology etc. of the Epidemic of Yellow Fever at Lisbon in* 1857, Blue Book, Lond. 1859, p. 45.

[‡] Alvarenga, *Anat. path. et symptomatologie de la fièvre jaune*, Transl. by Garnier, Paris, 1861, p. 65.

[§] Dutroulau, *Union méd.* 1859, t. i. p. 430.

[‖] A. Clark, *New York Medical Times*, 1853, May, p. 238. Quoted by Laroche, *op. cit.* vol. i. p. 404.

But a still more important change in the hepatic cells remained to be described; Claude Bernard asserts that all who went to Lisbon to study the recent epidemic of yellow fever (1857), were come back unanimous in their belief that the cells of the liver disappeared in this terrible malady.† Schmidtlein, who saw some part of the epidemic at Vera Cruz in 1865, examined the livers of five cases with the microscope; in four he found no traces of liver cells, but only a fatty detritus; in the remaining case the cells seen were much altered in their outline, and everywhere in the preparation were detritus and large and small fat drops.‡ And of late Lebrado has noticed that the not uncommon ending of parenchymatous degeneration in cirrhosis may take place also in yellow fever.§

Another important change in the liver has been found by Alvarenga. In nine cases of death from yellow fever not even a trace of sugar could be found in the liver. In another case, however, of rapid death from yellow fever a large quantity of sugar was found. Alvarenga is careful to point out that the nine patients in whom no sugar was found were taking the diet, and that this would account for the absence of sugar.‖ Still, the point is well worth bearing in mind when the absence of glycogen in acute yellow atrophy and phosphorus poisoning is considered.

The gall bladder is sometimes empty and contains an ill-coloured bile; or is filled with bile quite natural in appearance. Sometimes it is said to contain blood or thick grumous material.

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* Bache, *American Journal of Med. Sciences*, 1854, vol. xxviii, p. 124.

† Claude Bernard, *Leçons sur les liquides de l'Organisme*, Paris, 1859, t. ii. p. 212.

‡ Schmidtlein, *loc. cit.*

§ Lebrado, *Gaz. méd. de Paris*, 1877, p. 574.

‖ Alvarenga, *op. cit.*, p 70.

On reviewing the features of yellow fever as drawn by observers at the bedside and in the dead house, it is hard to avoid being struck with the resemblance which the disease bears, especially in the changes found after death, to some sporadic cases of what the French call *icterus gravis*, seen in these northern climates. It is almost impossible to distinguish between the report of the examination after death of a case of yellow fever and of acute yellow atrophy.

The state of the liver is the same in both, an acute fatty degeneration, or parenchymatous degeneration, attended with a solution or disappearance of the hepatic cells. The size of the liver in acute yellow atrophy depends upon the time of the disease at which the patient dies, as Liebermeister has pointed out; in yellow fever, death comes on so suddenly that there may be no time for a shrinking of the liver. In all other particulars the anatomical changes are also closely akin, the parenchymatous degeneration of the kidneys and heart, the acute catarrh of the stomach and intestines, the absence of glycogen from the liver, the hæmorrhagic diathesis. The only point in the two diseases in which a difference can be made out is the state of the spleen. This organ is, in yellow fever, rarely increased in size, while in acute yellow atrophy the enlargement is almost constant. It is possible that the time of the disease at which death takes place, may afford some explanation of this phænomenon.

The clinical features are less alike. But there are four common to both diseases: the jaundice, which cannot be denied; for if patients in yellow fever be not jaundiced, there is no other disease in which they are: the nervous symptoms, such as delirium, coma and convulsions: the hæmorrhagic diathesis: and the decrease of urea. There are also a few other symptoms sometimes, but not often, seen in both diseases; such as a roseolous or petechial rash; a high temperature before the onset of the jaundice; and the appearance of parotid bubo in cases which recover.

It cannot be said that the greater part of those authors who have spoken of the kinship of yellow fever to *icterus gravis* have looked with favour on the idea. Trousseau refuses to consider the question at all.* And Ozanam declares that those who speak of the identity of the two diseases, yellow fever and *icterus gravis*, fall into grave error.† Other writers speak with more hesitation.‡ Graves gives the name of yellow fever to an epidemic of jaundice, fatal in many instances, seen by him in Dublin, 1826:§ and Arnott of Dundee says that an epidemic noted by him in that place agreed so nearly with the symptoms during life, and the morbid anatomy after death, of the yellow fever of the West Indies, that little doubt was left on his mind that the difference was in degree and not in kind.‖

Rayer is said to have published two cases of *icterus gravis* from the Charité under the name of yellow fever;¶ and both Andral and Monneret looked upon the case of Siphnaios, a Greek medical student at Paris, who had symptoms of *icterus gravis*, but recovered, as one of yellow fever.** He made his own case the subject of his thesis. It is this case apparently which Griesinger has in mind when speaking of the relations of yellow fever and *icterus gravis*. "Many," he says, "but by no

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* Trousseau, *Clinique méd.* Paris, 1865, 2e éd. t. iii. p. 289.

† Ozanam, *De la forme grave de l'ictère essentiel*, Thèse de Paris, 1849, p. 9.

‡ Lebert (*Arch. f. path. Anat.* 1855, Bd. viii. p. 183.) allows the great resemblance, but denies the identity, of *icterus gravis* and yellow fever.

§ Graves, *Clinical Lectures*, Dublin, 1864, Neligan's edition, p. 213.

‖ Arnott, quoted by Graves, *op. cit.* p. 229.

¶ Rayer, *Gaz. des Hôp.* 1845, p. 369.

** Siphnaios, *Essai sur la fièvre jaune sporadique*, Thèse de Paris, 1852.

means all, look upon the cases seen
called *icterus gravis* as so near allied to
they call them by the same name."[*]
10 years after says he should not be at
one day it were proved that yellow fe
gravis were but two varieties of the same
the destruction of liver cells in yellow
been found because not looked for; but
is quite possible the diseases may be di
so alike:[†] opinions which I readily endo
draws attention to the connexion betwe
atrophy, yellow fever, and various other

Garnier did not hesitate to assert
identity of the two diseases.[§] Monne
so far, but expressed his belief that the
fever, the yellow fever of America, and
morrhagic jaundice *nostras* were only
same kind of disease; at least three
same kind united by two common chara
in the blood and troubles in the biliary s

Blachez, following the footsteps of
dorses much of the opinions of Monnere
his inaugural thesis, also gives us the vi
who would seem to believe that acute
of the liver and yellow fever are identical

But Liebermeister deserves the credi
first to draw a scientific comparison

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[*] Griesinger, *Infectionskrankheiten*, Erlangen, 1857, p. 82

[†] Grisolle, *Traité de Pathologie interne*, Paris, 1865, 9e éd

[‡] Buhl, *Zeitschrift f. rat. med.* 1854, Bd. iv. N. F. p. 355.

[§] Garnier, *Bulletin de l'Académie nationale de Méd.* 1850-

[||] Monneret, *De l'ictere hémorrhagique essentiel*, Paris, 18
from *le Journal de Progrès*. Cf. *Gaz. des Hôp.* 1862, p. 18
have been well if Monneret had only stated his opinions and
for them. The former we may agree with, while the latter

[¶] Blachez, *de l'ictère grave*, Thèse de Paris, 1860, p. 42.

[**] Proust, *du genre morbide ictère grave*, Paris, 1867. He
Pol Matthieu sustained a thesis at Paris in 1862 in which he
in the close kinship of these two diseases.

yellow atrophy and yellow fever.[*] He does not appear to have been aware of the observations reported by Claude Bernard; nor could he have known Schmidtlein's work, since it was not done until after the publication of Liebermeister's valuable volume: the greater credit is therefore due to Liebermeister in foretelling the complete agreement in morbid anatomy between the two diseases. Only I think that in asserting the complete identity of acute yellow atrophy and of yellow fever, he has gone further than the data supplied to us will allow. The two diseases undoubtedly belong to the same class, but I do not think the clinical history of the two is so completely alike as to justify an assertion that the diseases, alike as they are in many features, are really the same.

Happily in London we have had no opportunity of any extended observations on yellow fever, and the foregoing account of the disease is taken chiefly from Laroche's book on Yellow Fever, published in two volumes octavo at Philadelphia in 1855. This work has formed the basis for all descriptions of the disease which have been published since that date: it is the most complete account ever given to the world, and contains full bibliographical references up to date of publication. To the more important observations of the last 20 years I have given references in the notes to the pages above.

"BILIOUS TYPHOID."

This is a name used by Griesinger[†] for an epidemic disease seen by him in Ægypt, and which clearly belongs to the same class as yellow fever. Probably it is the same disease which has received in the Levant the name of *typhus icterodes*, and which was seen in the armies in the Crimea.

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[*] Liebermeister, *Beiträge zur pathologischen Anatomie u. Klinik d. Leberkrankheiten*, Tübingen, 1864, p. 261.

[†] Griesinger, *Infectionskrankheiten* in Virchow's *Handb. d. spec. Path. u. Therapie.* Erlangen 1857, p. 210. Cf. Lebert, in Ziemssen's *Handb. d. spec. Path. u. Ther.* Leipzig, 1874, Bd. ii. Theil i. p. 288. Lebert approves of the name "bilious typhoid," (p. 291.) which seems to me very unsuitable.

Griesinger believes it not to be contagious, but due to bad hygienic states, such as filth and misery generate. It attacked young people rather than old.

The picture given by Griesinger of the disease resembles yellow fever in its symptoms and morbid appearances so closely, that there can be little doubt that the diseases are closely allied, though not identical. The symptoms are alike in each; but the spleen in bilious typhoid is large, the Malpighian bodies are found suppurating, and there are pale wedge-shaped bodies, irregularly distributed through the spleen; an appearance which Griesinger thinks separates bilious typhoid altogether from yellow fever. The liver is pale, jaundiced, dry, and flabby, and in some cases resembles the state of acute yellow atrophy. The kidneys are swollen and fatty, and petechiæ and bleedings in other parts are always seen. Pneumonia and infarction of the lung are very common. The muscular tissue of the heart is flabby and pale. Griesinger does not seem to have used the microscope in his observations.

CHAPTER XXIV.

PHOSPHORUS POISONING.

THE jaundice seen in poisoning by phosphorus is an *icterus gravis*. Of late years the study of the phænomena of phosphorus poisoning has been forced upon physicians; on the continent it has become the fashion to commit self murder by means of this substance; and in a few years, from being one of the rarest poisons used, phosphorus has risen high in the statistics as a cause of death: a German physician acknowledges himself to be horrified at the number of persons killed by this means, seen every year at the Pathological Institute at Berlin. He says that scarcely a week passes but some bodies are brought for examination.* In England phosphorus poisoning is happily not so common; but its phænomena are highly interesting, not merely from the circumstance that some German pathologists attribute all cases of acute yellow atrophy of the liver to poisoning by phosphorus, but from the deep changes in nutrition throughout the body, which a grain or two of this substance may cause.

Phosphorus may be given as a poison in various ways. The method most commonly employed in Germany is to make an infusion in coffee of the heads of lucifer matches, from 100 to 1000 in number, and to take the mixture by the mouth. The allotropic form of phosphorus is not poisonous. Phosphorus is most active when administered in fine division. Large solid pieces may be given by the mouth, and passed out by the anus without causing serious discomfort. It is somewhat hard to estimate the smallest dose that may cause death. L. Hermann puts it at ·1 grm. to ·2 grm.[*] In English weights this would be about one and a half to three grains.

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* Nobiling, *Bayr. aerztl. Intelligenzbl.* 1870, No. 31, in Virchow and Hirsch's *Jahresb. f.* 1870, Bd. i. p. 268.

The cases of 11 men and 34 women poisoned by phosphorus, were collected or observed by Lebert and Wyss. The employments of the men were those of the lower orders of life, workmen, pedlars, one sailor, an apprentice, and a distiller. The women were domestic servants, needle-women, and others gaining their livelihood by the work of their hands; in one case a married woman, ill-treated by her husband.[†] Tüngel, writing in Hamburg, found that prostitutes formed one half of his cases;[‡] but in judging of this, there should be kept in mind the reputation of Hamburg, which, unless it be greatly belied, is somewhat unsavoury.

As regards the sex of the patient, women far more commonly poison themselves with phosphorus than men. Lebert and Wyss found that there were three women to every man both in their own cases and in those which they collected. Another curious fact brought out by these observers is the youth of the patients, which is well shown by the following table:

From 10 to 15	1
16 ,, 20	4
21 ,, 25	17
26 ,, 30	9
31 ,, 35	8
36 ,, 40	2
56 ,, 60	2
66 ,, 70	1
	44

Phosphorus poisoning is thus rare before puberty and attains its greatest height between 20 and 30. After 35 it becomes rare.[§]

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[*] L. Hermann, *Lehrb. d. exp. Toxicologie*, Berlin, 1874, p. 233.

[†] H. Lebert and O. Wyss, *Archives gén. de Médecine*, 1868, vol. ii. p. 260.

[‡] Tüngel, *Klinische Mittheilungen*, 1861, Hamburg, 1863, p. 125.

[§] Lebert and Wyss, *op. cit.* p. 259.

At Breslau, two thirds of the cases were seen in the winter from November to March inclusive. The three months of spring show the fewest; the autumn more.*

When a poisonous dose of phosphorus has been taken, there may be no symptoms for several hours. Sometimes, however, they come on sooner, even at the end of the first hour. There are burning pains in the epigastrium, sometimes in the pharynx, thirst, bad taste in the mouth, and lastly nausea and vomiting. These two last symptoms are very constant. In Lewin's early collection of cases he found vomiting spoken of in 26 out of 32 cases; vomiting and nausea together in 28 out of 32.† The vomited matters are the contents of the stomach and show the phosphorus which they hold by the peculiar smell or by shining in the dark. The breath may be phosphorescent from the retention of particles of the poison in the mouth or on the pharynx. At the end of ten to twelve hours the vomiting and pains in the stomach subside. The practitioner must be on his guard against this deceptive improvement. It is of course possible that the whole of the poison may have been rejected by vomiting, and uninterrupted recovery take place. But caution is especially needed as no forecast can be made from the amount of poison taken: a very little may have been swallowed and the whole of this very little seem to be rejected, and yet grave symptoms come on in three or four days; or a large quantity may be taken and yet no evil effects follow. Special care must therefore be taken at this stage in forming and expressing a prognosis.

At the end of three, four, or five days, grave symptoms are set up. The vomiting returns, but is less abundant and less violent than at first; and with the vomiting, the pains and tenderness of the epigastrium.

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* Lebert and Wyss, *op. cit.* p. 261.

† Lewin, *Arch. f. path. Anat.* 1861, Bd. xxi. p. 514.

The vomited matters now begin to change colour from the presence of blood. They are dark or chocolate coloured, or even show the appearance of unaltered red blood. Diarrhœa and colicky pains seem common, and are much oftener seen than constipation. The stools, according to Lebert and Wyss, are sometimes completely colourless; sometimes tinged by blood. These observers also assert that diarrhœa is wanting in one-third of the cases, and that the stools may within the first few hours be phosphorescent.[*]

Before the appearance of the graver symptoms, the liver, if carefully examined about the second day, will be found to be swollen in all dimensions. It next becomes tender. About the third day, as a rule, the jaundice begins. In some cases even earlier, on the second day, or even within the first twenty-four hours, as in Jacobsohn's case in which the jaundice was noticed 14 hours after the taking of the poison.[†] Bamberger asserts, however, that the jaundice may first appear as late as 14 or 21 days after the first ingestion of the phosphorus.[‡]

The jaundice and swelling of the liver gradually decrease if the patient be going to recover. In fatal cases the jaundice continues, ; opinions are divided if the liver decrease. Lebert and Wyss assert that there is a true atrophy of the liver;[§] Schultzen and Riess state that they were able in no case to detect any decrease of the liver dullness; and that in all cases in which this was supposed to have happened, the decrease of dullness was deceptive, owing merely to tympanites.[‖]

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[*] Lebert and Wyss, *Arch. gén. de méd.* 1868, vol. ii. pp. 265 and 708.

[†] Jacobsohn, *Deutsche Zeitschrift f. prakt. Med.*, 1874, p. 467 in Virchow and Hirsch's *Jahresb. f.* 1874, Bd. i. p. 454.

[‡] Bamberger, *Anzeiger d. kk. Gesellschaft d. Aerzte in Wien*, 1876, p. 130.

[§] Lebert and Wyss, *op. cit.* p. 709. These observers state, however, that the atrophy is not seen before the middle of the second week (p. 267).

[‖] Schultzen and Riess, *Annalen des Charitè Krankenhauses*, 1869, Bd. xv. p. 45.

In one, however, at least of Schultzen and Riess' cases the weight of the liver after death was reduced; it was 921 grm. (less than two pounds) in a girl of 22, with death on the 9th day after symptoms were first seen.* The size of the liver may possibly vary with the time of death after the poisoning.

The nervous symptoms which accompany phosphorus poisoning are seen not long after the jaundice has developed itself. But at first the patient shows that curious mental state which is present in many cases of self murder. After the jaundice has set in, a fresh set of nervous symptoms declare themselves. They begin about the fourth or fifth day; or may be delayed as late as to the tenth day, according to Lebert and Wyss.† Somnolence, increasing to coma, is broken by attacks of delirium, sometimes furious and maniacal. Later on convulsions and spasmodic movements are seen; the pupils become dilated, and the stools and urine are passed involuntarily.

It should be noted that, in some cases, no marked nervous symptoms are seen up to the moment of death. Insomnia is also sometimes, but rarely, noted.

The hæmorrhagic diathesis in phosphorus poisoning manifests itself during life chiefly by the presence of blood in the vomited matters, and in the stools. In the urine blood is rarely seen. Epistaxis is but little mentioned in the reports; and petechiæ, when spoken of, are in small number. The bites of leeches may give too abundant supply of blood.

According to Lebert and Wyss, the temperature is, as a rule, slightly raised, 38° to 38·5° C. (100·4° to 101·5° F.) In severe cases the temperature may be high 39° or 39·5° C. (102·2° or 103° F.) to sink to 36·5° or 35° C. when a fatal collapse shall come on (97·7° or 95° F.)

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* Iidem, *ibid.* p. 8.

† Lebert and Wyss, *op. cit.* p. 710.

The low temperatures which augur ill are seen oftenest from the fourth to the seventh day; while those of good omen appear from 8th to 10th day.

It has been already noted that at the approach of death from jaundice, the temperature may rise very high. The same holds true of phosphorus poisoning, where the temperature has been seen by Lebert and Wyss as high as 41·9° C. (107·4° F.[*]) Schultzen and Riess have observed the same appearance, but the temperature was much lower.[‡] These last observers say that the temperature in phosphorus poisoning follows no rule. Rommelaere has noted as a curiosity in one of his cases that the morning temperature was always higher than the evening.[§]

The pulse is somewhat increased at the beginning until the jaundice, when it falls. The fall is seldom very great, and the number of the beats not below 60 or 56. Later on, the pulse becomes feeble, small, thread-like in the fatal cases, but recovers its strength in those which recover. Schultzen and Riess note that the first sound of the heart becomes inaudible,[‖] as in the adynamic fevers.

In some rare cases a roseolous rash has been seen on the skin. Leube noticed an orange red exanthema, like nettle rash, on the skin of the epigastrium, thighs, and arms in a case of recovery.[¶]

It cannot be said that the urine in phosphorus poisoning received much attention until the analyses of Schultzen and Riess.[**] These observers find that the urine is singularly uncertain in its composition: still however, its state corresponds so far to the clinical appearances that an unfavourable course of the poisoning and severe symptoms coincide with great changes in the urine. The urine is always acid. Its specific gravity varies from 1016 to 1020. Lebert and Wyss think that the specific gravity decreases after the jaundice comes on, being then 1008 to 1016; before, they have noted it from 1028 to 1032.* The quantity decreased with the increase of the severe symptoms, so that it may fall as low as 80 or 100 C.C. in the last 24 hours. There is never, however, a true anuresis.

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[*] Lebert and Wyss, *op. cit.* p. 275.

[‡] Schultzen and Riess, *op. cit.* pp. 24 and 46.

[§] Rommelaere, *Bulletin de l'Académie de méd. de Belgique*, 1872, t. v. p. 1043, in Virchow and Hirsch's *Jahresb. f.* 1872, Bd. i. p. 343.

[‖] Schultzen and Riess, *op. cit.* p. 45.

[¶] Leube, Virchow and Hirsch's *Jahresb. f.* 1874, Bd. i. p. 454.

[**] Schultzen and Riess, *op. cit.* p. 53.

Albumen is not always found. It is present only in small amount. Bile pigments and bile acids in quantity were found whenever looked for. Lebert and Wyss find albumen almost constant; at all events as often as bile pigment; while the bile acids are found seldom and in small quantity, more often in dogs than in men.

As soon as the jaundice, swelling of the liver, and feeble action of the heart set in, the amount of urea falls very considerably; and in place of the urea, other nitrogenous bodies appear. If the patient be going to recover, these bodies in their turn disappear and the urea comes back in natural amount. But if the case will end fatally, then the urea sinks to a *minimum*, without however disappearing altogether.

Lebert and Wyss seem to have paid but little attention to the amount of urea. In one of Alter's experiments on dogs, a biliary fistula was set up in December 1866. The dog was poisoned three times; on January 19, 1867, February 20, and February 26. He died the next day. On February 25 and 26, the urine contained 4·92 and 6·2 of urea, in 35 C.C. and 140 C.C. of urine respectively. The weight of the animal is not given, nor is it stated whether the whole of the urine was collected, or the method by which

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* Lebert and Wyss, *op. cit.* p. 268.

the urea was estimated.* Joseph Baue
a dog for seven days. On the first
the urea was 20·7 grammes; on the s
throughout the rest of the time that it w
was commonly lower than this. On
1·5 grain of phosphorus was given; or
urea had risen to 12·7 grm. on the tent
The estimation was, however, made by I
which Schultzen and Riess consider u
phorus poisoning, a peptone being prese
A second dog was therefore starved for
like result of a rise in the amount of ur
estimated by Liebig's method, and the
nitrogen present in the urine, estimate
lime process, corresponded very closely
of nitrogen in the urea estimated by Li
So that Bauer seems to think that th
nitrogen must have come from urea
which I venture to think rather doubtful.

The amount of creatinin decreases *pa*
urea, and when only traces of urea car
traces of creatinin are found likewise.
Schultzen and Riess' which recovered,
companying the sudden rise in the urea
quantity of three grammes of creatinin i

The uric acid does not disappear alto
cases of intense poisoning. Schultzen a
it may be increased, but they have made
on this point.

In the first dog of Bauer, there was so
the amount of phosphoric acid in the uri
became high. On the first day of hu

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* Lebert and Wyss, *op. cit.* p. 534. Munk and Leyden
Vergiftung, Berlin, 1865, p. 54) quote Wyss as finding neit
leucin and tyrosin in the urine of man. (from *Schweiz. Zts*
p. 321—325).

† Joseph Bauer, *Zeitschrift f. Biologie*, 1871, Bd. vii. pp.

phoric acid was 6·04; the six following days it never rose above 1·54. On the second day of phosphorus poisoning it rose to 2·77, on the third 3·76, to sink on the fourth to 1·9.[*] I can find no other estimations of the amount of phosphates in the urine; a somewhat surprising matter, as it would be interesting to know if they be always increased.

It is well known that the amount of extractive matter present in the urine of health is a mere trace, so small that it may be safely disregarded in estimating the amount of nitrogen. In phosphorus poisoning, however, the amount is greatly increased and the extractives insoluble in alcohol contain bodies like peptones.

Before these peptones and other extractives have appeared, the urine always contains its normal amount of hippuric acid. As soon, however, as the urea decreases and the extractives appear, the hippuric acid can only be found in traces, but sarcolactic acid in more or less notable quantity is present. In none of the cases which recovered was sarcolactic acid found, even if the peptones were already present in the urine.

As to the appearance of leucin and tyrosin in the urine, observers are divided. Schultzen and Riess deny the presence of these bodies in the urine, although they acknowledge that they found tyrosin in two experiments in the blood of a dog.[†] Lebert and Wyss found tyrosin in the urine, once in man, once in a dog: leucin once in the blood of a dog.[‡] Leube says that he has found tyrosin,[§] Ossikowsky leucin and tyrosin in the urine.[||] Tüngel states that he twice found with the microscope a few balls of leucin in the urine,[¶] and

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[*] Bauer, *loc. cit.*

[†] Leube, Virchow and Hirsch's *Jahresb. f.* 1874, Bd. i. p. 454.

[‡] Ossikowsky, *ibid. f.* 1870, Bd. ii. p. 169.

[§] Schultzen and Riess, *op. cit.* p. 96.

[||] Lebert and Wyss, *op. cit.* pp. 269 and 279.

[¶] Tüngel, *Klinische Mittheilungen*, 1861, Hamburg 1863, pp. 134 and 139

Kohts in his experiments on dogs found with the microscope numerous crystals of leucin and tyrosin, but they were too small in quantity for a chemical analysis.[*] J. Bauer once found by Hofmann's reaction a small quantity of tyrosin in the urine of a dog poisoned by phosphorus, but it was certainly absent from the urine both before and after.[†] It will be seen that of all these observers it is Wyss[‡] and Bauer only who have determined by chemical analysis the presence of tyrosin in the urine. The diagnosis of the others rests upon the microscope. Schultzen and Riess, examining carefully in a chemical laboratory, were unable to find either tyrosin or leucin.

In no case did Schultzen and Riess find sugar in the urine.[§]

Lebert and Wyss note the presence of pale casts, rarely granular,[‖] and Tüngel of casts and epithelial cells tinged by pigment,[¶] appearances which might be looked for, the state of the kidneys being given.

The changes in the state of the blood, early attracted notice. The blood is thin and seems to lose its power of coagulation, a circumstance of which Schiff has proposed to avail himself in making manometrical observations.[**] Doubtless this is some explanation of the severity of the bleedings when once they are set up. After death dark clots are usually found in the heart, rarely fluid blood. It was formerly stated that the red corpuscles were found dissolved in the plasma,[††] but this has long been discredited; and Lebert and Wyss, agreeing with many other writers, state that the red

[*] Bauer, *op. cit.* p. 73.

[†] Kohts, *Deutsches Arch. f. klin. Med.* 1869, Bd. v. p. 185.

[‡] Wyss, Canstatt's *Jahresb. f.* 1864, Bd. v. p. 103.

[§] Schultzen and Riess, *op. cit.* p. 57.

[‖] Lebert and Wyss, *op. cit.* p. 269.

[¶] Tüngel, *op, cit.* p. 134.

[**] Schiff, *Arch. f. exp. Path.* 1874, Bd. ii. p. 345.

[††] Casper, *Handb. d. ger.-med. Leichen-Diagnostik*, Berlin, 1857, p. 441.

corpuscles are unchanged in phosphorus poisoning.[*] Rommelaere agrees to this: but notes that he found a few granular and indented corpuscles; a mere *post-mortem* phænomenon. The white corpuscles were also greatly increased.[†] Ménard found the amount of fat in the blood greatly increased, 3·41, 3·52, and 3·73, *per cent.* instead of 2·05 *per cent.* in healthy dogs. Under the microscope the blood showed, in proportion to the intensity of the poisoning, stellate or needleshaped crystals, soluble in æther. These crystals do not arise from the solution of the blood corpuscles, which Ménard found natural save a fine granulation. They seem rather to be due to some change in the blood which is the first result of the poison, and to which Ménard thinks the hæmorrhages and jaundice are due.[‡]

Schultzen and Riess twice found by chemical analysis tyrosin in the blood of dogs poisoned by phosphorus[§] and Lebert and Wyss leucin.[||]

The body of a person poisoned by phosphorus shows no marks of putrefaction. This is the more noteworthy, as it has been stated that an increase of the putrefactive ferment is most often noticed where the earthy phosphates are present in abundance.[¶] A general jaundice is present. A multitude of ecchymoses in the serous and mucous membranes is seen, most abundant on the pericardium, endocardium, pleuræ, and peritonæum. They are also often seen in the planes of the connective tissue.

The cause of the hæmorrhagic diathesis seen in phosphorus poisoning is most probably due to the fatty degeneration of the small arteries and capillaries, and not to any primitive change in the blood itself. The existence of this fatty degeneration has been pointed out by Klebs in the vessels of the subcutaneous connective tissue[*] and by Bollinger in those of the lung.[†]

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[*] Lebert and Wyss, *op. cit.* p. 279.

[†] Rommelaere, Virchow and Hirsch's *Jahresb. f.* 1872, Bd. i. p. 343.

[‡] Ménard, *ibid. f.* 1869, Bd. i. p. 327.

[§] Schultzen and Riess, *op. cit.* pp. 108 and 110.

[||] Lebert and Wyss, *op. cit.* p. 279.

[¶] Jules Lefort, *Bulletin de l'acad. de méd.* 1874, p. 141.

The brain shows very few alterations, and these chiefly in the meninges, from the presence of extravasated blood.

The heart suffers grave changes. The muscular tissue is pale, flabby, mottled grey and yellow. Under the microscope, the fibres show a complete granular or fatty infiltration of the fibres, with decrease or loss of the transverse striation. The degeneration seems to take place on both the right and left side in an equal degree, although Eulenburg and Landois found it more pronounced in the right than the left ventricle.[‡] The same change may be noticed in the voluntary muscles of the rest of the body, the chest, belly and limbs; the waxy change described by Zenker being rarely seen, and then in but few fibres.

The lungs offer no remarkable changes to the naked eye; there do not seem to be reported any instances of pulmonary infarction, as there are in some kindred cases. The epithelium of the bronchi has been noticed by Bollinger to be so filled with fat that it resembled the cells taken from an ordinary fatty liver, rather than the epithelium of the air tubes. The vessels were also found in a state of cloudy swelling.[§]

The spleen is often found enlarged to double its natural size, and its consistence decreased; sometimes it remains quite natural.

Since the time of von Hauff,[‖] the liver has always been looked upon with some attention, and now perhaps it is the organ of all others which the morbid anatomist investigates with the greatest interest.

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[*] Klebs, *Arch. f. path. Anat.* 1865, Bd. xxxiii, p. 443.

[†] Bollinger, *Deutsches Arch. f. klin. Med.* 1869, Bd. v. p. 153.

[‡] Eulenburg and Landois, *ibid.* 1867, Bd. iii. p. 451.

[§] Bollinger, *loc. cit.*

[‖] Von Hauff, *Würtemb. Corr.-Bl.* 34, 1860. Abstract in Canstatt's *Jahresb. f.* Bd. v p. 114.

The liver is, as a rule, increased in size, quite smooth on the surface, sometimes showing old adhesions to the diaphragm. Rarely it is decreased in size, and this is seen only at the end of a prolonged poisoning: and Lebert and Wyss say that it then shows the characters of the liver seen in acute yellow atrophy. They have once seen it weigh as little as 700 grammes.* Schultzen and Riess say they have only once seen the liver decreased in weight, and then it was 920 grammes.† Setting these rare cases aside, the changes in the liver seen with the naked eye seem to be tolerably constant. They are those which may be described as characterising the well-marked fatty liver.

Over the histology of the liver, there has been much disputing. Schultzen and Riess describe the liver in the following terms: "in all our cases, saving the first, the liver, as also in the more part of the cases known, was strikingly increased in size and doughy to the feel; the surface, as the section, uniformly bright yellow, the latter shining with fat, and greasing the knife; in the parenchyma, uniform in colour, there showed very plainly, through the red network of the interlobular and intralobular vessels, lobules strikingly large, while the larger vessels and the capillaries of the lobules were empty of blood. In short, the appearance of the liver was, as also has been set forth by most observers before us, that of a far advanced fatty liver, markedly jaundiced, only more so than the ordinary fatty liver is. Examination with the microscope confirms this appearance; there are found, without exception, liver cells markedly fatty, and indeed, for the most part, filled with large fat drops, and so swollen, that they were in part thought to be mere collections of such drops (at least these were seen in all our cases.) The cells lying in the neighbourhood of the portal vein are usually those most advanced in the degeneration; in many of our cases the periphery of the acini were filled with free fat drops lying close to one another, while in the zone of the central vein, the cell outline was still visible around the fat drops. In these cases the cells of the central part often held abundance of biliary pigment, an appearance which, however, is not constant in the liver of phosphorus poisoning."[*]

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* Lebert and Wyss, *op. cit.* p. 283.

† Schultzen and Riess, *op. cit.* p. 47.

These observers could find no change in the connective tissue by any method of preparation; and their description of the liver in phosphorus poisoning seems to me agreeable to that given by most observers. Winiwarter, for instance, says that the resemblance of the liver to ordinary fatty liver is so complete that he could not trust himself to distinguish the one from the other under the microscope.[†] But so early as 1863, Mannkopff met with quite a different state of the liver.[‡] His description recalls very closely Zenker's account of acute yellow atrophy. There were two differently coloured tissues in the liver, the yellow and the red, the red depressed below the surface of the yellow. The yellow is the first stage, of which the red is the second stage. The yellow parts showed the acini large and, easily distinguished from one another. Under the microscope the cells appeared filled with fine fat, and, around the central vein of the lobule, with brown pigment. Around the circumference of the lobule the connective tissue could be seen broader than natural, and, between the fibres, a large number of connective tissue nuclei. In the red part, the lobules also appear large and easily distinguished, but they were marked out by broad bright bands. The consistence of the red parts was less than that of the yellow. With the microscope liver cells could no longer be seen, only nuclei and free fat, but there was great increase of the connective tissue starting from the portal vein.* Ludwig Mayer describes the liver in his cases as having the appearance of a fatty liver with early cirrhosis†; and Oskar Wyss, in several men and dogs, found an overgrowth of the connective tissue.‡

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[*] Schultzen and Riess, *op. cit.* p. 47.

[†] Winiwarter, Stricker's *Med. Jahrbb.* 1872, p. 268.

[‡] Mannkopff, *Spitals-Zeitung*, Beilage zur *Wiener med. Wochenschrift*, 1863, p. 349.

With these views Lebert and Wyss agree. They allow that the liver is increased in size in the greater number of cases, but that, should the poisoning last longer than is customary, the liver then becomes shrunken, and consistence flabby. Sometimes the liver shows a likeness to the common fatty liver, but more often the surface offers an unequal discoloration, the lobular islets white, yellow-white, or jaundiced. In certain cases, however, the colour is a brown-red, verging upon yellow or grey. The vascular distribution of the surface is also very unequal. On the cut surface the same characters are seen, but the lobules are more easily recognised. At a degree less advanced the red tint in the centre of the lobules persists, while the circumference is pale, or grey-yellow, or jaundiced. Later on the yellow tint is seen all over the lobule, and the distinction between the lobules is effaced; the consistence is sometimes decreased, and the section becomes granular. These two observers have sometimes seen the lobules surrounded by a grey line from 1 to ·5 millimeter in breadth. With the microscope the cells are first seen simply increased in size, filled with very small but abundant granules, so as to show a cloudy, almost opaque appearance. This state is not found everywhere in the liver, but disseminated in small tracts. Then instead of granules, larger and larger drops fill the cells, the cell-wall disappears, then the nucleus goes, and there is nothing left but a collection of globules of fat. The grey line, which surrounds the lobules, shows under the microscope an undoubted hyperplasia of the connective tissue, and its corpuscles. This is, however, an appearance of some rarity.[*] Georg Wegner found, by poisoning animals very slowly with very small doses of phosphorus, that the liver, although increased in size, became increased in consistence; and that the connective tissue of the portal canals showed an active cell growth, and that a firm fibrous connective tissue was formed between the acini. The cells in the circumferential part of the lobule are destroyed by fatty metamorphosis, plainly, says Wegner, from pressure. In short, an interstitial hepatitis *in optima forma* is seen, ending in a well-marked cirrhotic liver.[†] The animals die from portal congestion, hyperæmia of the stomach and intestines, indurative enlargement of the spleen, ascites and hydrothorax. Much the same appearances were seen by A. Weyl.[‡]

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* Mannkopff, *op. cit.* p. 332.

† Ludwig Mayer, *Arch. f. path. Anat.* 1865, Bd. xxxiii. p. 299.

‡ Oskar Wyss, *ibid.* p. 432.

On reviewing the facts before us, I think it must be granted that the liver in poisoning by phosphorus may take two forms; one in which the cells are the structures chiefly involved; another in which the connective tissue as well as the cells are attacked. Whether the connective tissue shall increase seems to be determined by the length of time which the poisoning lasts, and the smallness or largeness of the doses, and if repeated or given once for all. If this be the true way of looking at the matter, the effects of phosphorus closely resemble those of alcohol. An acute poisoning by alcohol causes a granular or fatty infiltration of the liver; a chronic poisoning, a cirrhosis.

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[*] Lebert and Wyss, *op. cit.* pp. 283-285.

[†] Georg Wegner, *Arch. f. path. Anat.* 1872, Bd. lv. p. 19.

[‡] A. Weyl, *Arch. d. Heilkunde*, 1878, Jahrg. xix. p. 163.

It will be convenient here to discuss the cause of the jaundice. It was formerly thought, and indeed the position has its defenders now, that the jaundice was due to some change in the blood, probably the direct work of the phosphorus itself. The ducts were thought to be free from obstruction, and to contain bile. How then could there be a mechanical cause for the jaundice? Oskar Wyss has answered this question very satisfactorily. He made biliary fistulæ in dogs, and then poisoned the animals with phosphorus. Very little bile flowed out of the fistulæ, and yet the dogs became jaundiced. This at first sight could be taken for evidence that the liver ceased to secrete bile, and that it accumulated in the œconomy, bringing forth jaundice. But on dissecting the liver, the large ducts were found to be unstained, while the openings of the smaller ducts were plugged with a thick mucus which hindered the flow of the bile into the larger tubes.* Ebstein, too, has noticed a like appearance in the livers of men poisoned with phosphorus.† Schultzen and Riess, on the other hand, say they have been unable to find appearances such as those which have been noted by the foregoing writers.‡ Notwithstanding this statement, it is most likely that the jaundice is due to some obstruction in the hepatic ducts high up in the liver, as Wyss has pointed out.

It is important to note that the liver was found free from sugar in two of Schultzen and Riess' cases,§ and that Saikowsky found that in 24 to 36 hours after poisoning with phosphorus, the glycogen had completely disappeared from the liver in young rabbits: if, however the animals were old, glycogen was still present, but in much decreased amount.[*]

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* Oskar Wyss, *Arch. d. Heilkunde*, 1867, p. 469.

† Ebstein, *ibid.* 1867, p. 506: and 1869, p. 579.

‡ Schultzen and Riess, *op. cit.* p. 50.

§ Schultzen and Riess, *op. cit.* pp. 14 and 43.

In the old descriptions of the mucous membrane of the stomach, ulcers and sloughs are very prominent.

It is rare, however, to meet with such: Rokitansky states that he has never met with ulceration,[†] the stomach merely shows the appearances of a catarrh, which extends also into the duodenum and intestines and may play an important part in causing the jaundice by filling the papilla with a plug of mucus and hindering the descent of the bile. The mucous membrane is swollen, opaque, cloudy; and under the microscope the peptic glands show a most striking fatty degeneration. Virchow was the first to point this out,[‡] but it cannot be regarded as pathognomonic of phosphorus poisoning, as it is present in acute yellow atrophy and doubtless in all other cases in which an acute parenchymatous degeneration of all the glands is present.

Next to the liver, the kidneys are the organs most commonly and most deeply affected. They are enlarged, though this appearance may sometimes be absent. The capsule tears off easily, leaving a surface mottled with unequal vascular distribution. The cortex itself is broadened, and pale, with a jaundiced tinge, the Malpighian bodies showing themselves as red points, while the purple medulla is markedly distinct from the paler cortex. Under the microscope the epithelium of the tubules is found filled with larger or small drops of fat, just in the same manner as the liver cells. The epithelium is indeed sometimes destroyed. In the medulla the intensity of the process is always less. The interstitial tissue is nowhere developed.

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[*] Saikowsky, *Arch. f. path. Anat.* 1865, Bd. xxxiv. p. 79.

[†] Rokitansky, *Anzieger d. kk. Gesellschaft d. AA. zu Wien*, 1876, p. 131.

[‡] Virchow, *Arch. f. path. Anat.* 1864, Bd. xxxi. p. 399

It is still uncertain whether phosphorus acts as phosphorus alone, or in combination with other elements. It has been said since the time of Magendie* that the *oleum phosphoratum* did not act when injected into veins. Some observers believe that the active agent is phosphoretted hydrogen; others, some compound with oxygen, as phosphorous and phosphoric acid. On the other hand some maintain that the phosphorus is absorbed, as such, in solution in the fats of the blood. This view is strengthened by the aggravation of symptoms which follows the ingestion of fatty matter after phosphorus poisoning.

Diagnosis. The diagnosis of phosphorus poisoning must depend greatly on the history. If the case be seen early, it may be possible to detect the presence of phosphorus in the vomited matters by their shining in the dark; or the breath may be phosphorescent. But if, as is commonly the case, the patient be not seen till the first symptoms have passed off, the diagnosis will be very hard to make. There appear to be no certain means during life by which phosphorus poisoning can be distinguished from acute yellow atrophy, or the subacute poisoning by arsenic, antimony, alcohol and a variety of other bodies. After death, phosphorus may be found in the blood, liver, and other organs, if the poisoning have run a rapid course, but at the end of a few days it cannot be detected. In acute yellow atrophy, the liver is commonly small; in phosphorus poisoning, large. In acute yellow atrophy, again, the liver is mottled red and yellow, the distinction between the acini lost, the cells broken down and those remaining infiltrated with fine granules; in phosphorus poisoning the liver has usually the appearance of a fatty liver, uniformly yellow, the acini well marked and large, the cell wall preserved, as may be seen after treating the section with æther, and the cells filled with large oil drops. But in some cases, even after death, it would appear that the diagnosis from acute yellow atrophy is uncertain, if not impossible. From antimony and arsenic poisoning it may be distinguished by the finding of these metals in the viscera.

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* The reference given by some is to the *Mém. de l'Institut* for 1811. But I cannot find the statement there nor can I find anything bearing on this in the long list in the Royal Society's catalogue of articles published by Magendie. Hermann and Brunner (*Arch. f. d. ges. Phys.* 1870, Bd. iii. p. 1) say that phosphorus does act when injected into the veins.

The prevalence of an epidemic, and the clinical symptoms, may serve to distinguish yellow fever from phosphorus poisoning during life. After death the points of separation are very obscure.

Prognosis. The chances of recovery vary from one half to a quarter of all cases seen, according to Lebert and Wyss.* The practitioner should be most guarded in forming a prognosis, and no favourable opinion should be given from the smallness of the dose. If speedy vomiting take place and the poison be speedily and entirely rejected, there is of course a better chance for the patient; also if the poison have been given in a watery infusion, and no fatty matters given with or after it. When the graver symptoms set in, jaundice, delirium, coma, hæmorrhages, and the like, the prognosis is still more serious, though recovery may possibly take place even under these unfavourable conditions.

Treatment. The treatment of phosphorus poisoning must be directed at first to the getting rid of the poison out of the body as quickly as may be. This seems best effected by prompt vomiting; and the emetics which may best serve this purpose appear to be ipecacuanha and mustard. Antimony seems to me objectionable for as much as its action is so closely allied to that of phosphorus. Bamberger recommends on theoretical grounds the use of the sulphate of copper.[*] Later on, if the vomiting prove obstinate, iced water, iced seltzer water, iced champagne if the patient be weak, may be used; so mustard poultices to the epigastrium, or if the pains be severe, the subcutaneous injection of morphia. Formerly calcined magnesia was given with a view to the oxydation of the phosphorus, and the formation of a harmless phosphate of magnesia. Of late years oil of turpentine has been much praised, being first brought forward by Andant who noticed that a man who took phosphorus and turpentine together suffered no serious disturbance.[†] All oily or fatty matters, milk and eggs, must be forbidden with the greatest severity. Persons, who have shown no serious symptoms up to the taking of fatty food, have been known to fall ill shortly after, and to die.

The amount of oil of turpentine to be given should be about a hundred times as much as the phosphorus taken; it is better given in capsules, not in any case in yolk of egg, on account of the fat therein present. Some recommend the *ol. terebinth. gallicum* alone as an antidote.

Eulenburg and Landois have recommended transfusion of blood in phosphorus poisoning,[‡] and this has actually been done by Jürgensen without any ill effects, although it must be owned that it was two months after the poisoning.[§]

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[*] Bamberger, *Würzb. med. Zeitschrift*, 1866, Bd. vii. p. 57.

[†] Andant, *Bulletin gén. de thér.* 1868, t. lxxv. p. 269.

[‡] Eulenburg and Landois, *Deutsch. Arch. f. klin. Med.* 1867, Bd. iii. p. 440.

[§] Jürgensen, *Berlin. klin. Woch.* 1871, p. 241.

CHAPTER XXV.

JAUNDICE AFTER POISONING BY ARSENIC, ANTIMONY, AND OTHER BODIES.

POISONING by phosphorus may be taken as the type of many other inorganic poisons; especially of those bodies which are so near in their chemical relations as arsenic and antimony. If a subacute poisoning with either of these bodies take place, jaundice may come on,[*] accompanied by nervous symptoms and hæmorrhages:[†] and after death, a parenchymatous degeneration of the liver and kidneys, heart and muscles may be found.[‡] The liver, as in phosphorus poisoning, ceases to contain glycogen.[§] The urea, however, does not seem to be decreased; neither are peptones nor sarcolactic acid found in the urine.[||]

Besides these, there are several others, organic and inorganic, which have in some respects a similar action, that is, they cause a parenchymatous change in the liver, kidneys, and muscles, and the cause of the jaundice is no doubt the same as in phosphorus poisoning.

i. A jaundice, it is well known, often arises after the inhalation of chloroform. The like has been noticed of æther; and the use of hydrate of chloral is thought by some to be also followed by jaundice.[¶] Leyden thinks the jaundice due to the action of the chloroform and æther on the blood corpuscles, which are said to be dissolved by these agents.[*] Wertheimber rejects this view, and proposes a theory that the jaundice is due to a paralysis of the bile ducts.[†] For my own part I feel inclined to attribute the jaundice to the same causes as in *icterus gravis*, for Nothnagel has shown that most extensive fatty infiltration of the liver, kidneys, and heart, rapidly follows the administration of æther or chloroform.[§] The same change has been found after chloral.

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[*] Vaudrey, Virchow and Hirsch's *Jahresb. f.* 1871, Bd. i. p. 312.

[†] Martineau, *Union méd.* 1873, t. xv. p. 558.

[‡] Munk and Leyden, *Berlin. klin. Wochenschrift*, 1864, p. 469. They find (p. 482) that all poisons which dissolve the blood corpuscles cause a fatty degeneration of the tissues and organs. See a case by Grohe and Mosler (*Arch. f. path. Anat.* 1865, Bd. xxxiv. p. 208) in which arsenic was found in the vomit, none in the body: yet well-marked fatty degeneration.

[§] Saikowsky, *Arch. f. path. Anat.* 1865, Bd. xxxiv. p. 73.

[||] Gähtgens, *Centralblatt f. d. med. Wiss.* 1875, p. 529.

[¶] Pelman, *Irrenfreund*, 1871, quoted by Arndt, *Arch. f. Psych. u. Nervenkrankheiten*, 1872, Bd. iii. p. 677. Wernich, *Deutsches Arch. f. klin. Med.* 1872, Bd. xii. p. 32.

Pelman[§] and Dr. Crichton Browne[||] both saw hæmorrhages follow the use of chloral. In Pelman's fatal case, the stools were nearly white, and yet no cause for this could be made out; the tissue of the liver was firm, dry, bloodless, and hard as leather, and Pelman thinks it due to a dissolution of the blood. In Wernich's cases, as much as three grammes (45 grains) of chloral seem to have been given, and were followed by jaundice, in one case of a deep olive green. In another of these cases there was violent delirium, and the diagnosis of acute yellow atrophy was made. In the fatal cases examined, the liver cells showed distinct fatty infiltration.

ii. Inorganic poisons, such as mercury and copper, are thought to bring on jaundice. Jaundice following mercury must have been more common when it was the custom to "throw in" this drug for the treatment of syphilis. Sir Henry Marsh has recorded a fatal case which happened in Dr. Colles' practice:[¶] calomel had been given four or five weeks for a chancre on the *glans penis*. About three weeks afterwards, this young man was observed to be deeply jaundiced, and having continued two or three days in this state, he was seized suddenly with delirium, followed by repeated convulsions. After death every viscus in the body was most accurately examined, and not a trace of disease could be discovered. The external and internal parts were much tinged with bile.[*] The case is not uncomplicated, as the actions of syphilis and mercury were both present together; and the fatal result may be set down to one, or the other; or a third cause. The same may be said of Rampold's fatal case: a servant girl was treated for syphilis with calomel. She became yellow, and died on the fifth day, delirious. The liver was small, and so soft that the finger could be readily pressed into the tissue.[†]

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[*] Leyden, *Beiträge zur Pathologie des Icterus*, Berlin, 1866, p. 6.

[†] Wertheimber, *Fragmente zur Lehre vom Icterus*, München, 1854, p. 12.

[‡] Nothnagel, *Berliner klin. Woch.* 1866, p. 31.

[§] Pelman, *loc. cit.*

[||] Crichton Browne, *Lancet*, 1871, Vol. i. p. 473.

[¶] Graves remarks upon the enlargements of the liver commonly following an injudicious course of mercurials. (*Clinical Lectures*, Dublin, 1864, p. 343.)

The physiological action of lead, copper, and silver is very nearly the same. One of the effects of silver has been shown by Bogoslowsky to be a cloudy swelling of the liver and kidneys, and a disappearance of the transverse striation of the fibres of the heart, and their replacement by granules.[‡] I am not, however, aware of any case in which jaundice has followed the use of silver. There are cases recorded of this symptom appearing in the chronic poisoning of lead[§] and of copper.[‖] In Stoll's case, a young woman of 20 took copper vitriol in order to bring on a miscarriage. Soon after, she became intensely jaundiced, with great pains in the epigastrium, and having aborted, died. The liver was found as soft as the lungs of healthy persons, the ducts free, and the gall bladder full of bile. Charcot reports a case of acute yellow atrophy in an epileptic who had long taken oxide of zinc. In the liver a large amount of zinc was found.*

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[*] Marsh, *Dublin Hospital Reports*, 1822, Vol. iii. p. 278. A case of Schönlein's appears to have been ordinary cirrhosis. (*Klin. Vorträge*, Berlin, 1842, p. 308.)

[†] Rampold, *Heidelb. Annal.* 1846, xii. 2, from Schmidt's *Jahrbb.* 1847, Bd. liii. p. 53.

[‡] Bogoslowsky, *Arch. f. path. Anat.* 1869, Bd. xlvi. p. 409.

[§] A. de Haen, *Rat. Medend.* Viennae, 1765, Pars x. p. 101. Cf. Gubler, *Union méd.* 1857, p. 503. Dreyfus-Brisac, one of Gubler's disciples, has collected 11 cases of lead poisoning complicated by jaundice. (*De l'ictère hémaphéique*, Paris, 1878, p. 49.)

[‖] Stoll, *Rat. Med.* Viennae, 1780, Pars iii. p. 390. Cf. Chaumel, *Gaz. d. Hôp.* 1863, p. 308. This case is complicated by pyæmia.

JAUNDICE AFTER POISONING BY ALCOHOL.

The effects of subacute poisoning by alcohol have a close resemblance to what is seen in poisoning by phosphorus, antimony, and arsenic. There are but few cases of subacute poisoning by alcohol on record, but Liebermeister has described one in which the symptoms, with the exception of an early attack of delirium, might have been taken for those of poisoning by phosphorus. The man, 37 years of age and a brewer, was accustomed to drink a great deal, and had suffered several attacks of *delirium tremens*. After a great excess he was seized in the night between 19th and 20th of February, 1863, with a violent attack of vomiting, and pains in the epigastrium. There was also delirium, like the former attacks, with great shortness of breath. Four days after, however, the man thought himself quite well; but the conjunctiva was yellow; and the next day there was jaundice of the whole body: there was then found out a great enlargement of the liver, reaching to the navel. On this day also vomiting again appeared. On the 6th day of the disease, violent delirium was noticed with maniacal outbreaks, pulse 140. On the morning of the 7th day, complete coma with stertorous breathing: death about midday.

After death, a very small part of the right lung was found in a state of grey hepatisation. Left lung natural. Heart large, some old adhesions in pericardium. Spleen large, soft. Liver much smaller than was looked for. In the rest of the organs no changes visible to naked eye. No hæmorrhages. The surface of the liver yellow-red with faint markings of the lobules; cut surface, uniformly orange red, no distinction between lobules: no blood comes from the cut surface. Consistence soft, doughy, but withal tough. Under the microscope not a single liver cell could be made out; only an immense number of fat drops, large, small, and small as granules. The connective tissue of the liver was also covered with fat drops. The liver contained no sugar, but leucin, tyrosin, and xanthin.[*] A case somewhat like this in its clinical features has been noted by Horaczek, but after death there can be no doubt from his description that the liver was cirrhotic. The microscope, as might be looked for at that date, was not used.[†]

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* Charcot, *Leçons sur les maladies du foie*, Paris, 1877, p. 82.

Leyden has noted that if jaundice complicate *delirium tremens*, the disorder nearly always proves fatal; and yet neither *delirium tremens*, nor jaundice, is by itself a severe illness; the greater number of cases of both these diseases recover. Leyden believes that the presence of the bile acids in the blood destroys a number of red blood corpuscles, and thus acts like blood-letting on the patient, the danger of which in *delirium tremens* is well-known.[‡]

It may be convenient here, in describing the *icterus gravis* caused by alcohol, to speak of the jaundice seen in drunkards, and which jaundice seems due directly to the alcohol. I do not of course intend to include the jaundice seen in cirrhosis. This jaundice follows an excess, not at once, but in a few days, and would appear to be due to the extension of the gastric catarrh, which is so common a consequence of alcohol poisoning, into the duodenum, and an obstruction of the duct as it passes into the gut. This jaundice does not last much longer than a fortnight; when recovery takes place. It would seem to bear the same relation to the *icterus gravis* caused by alcohol, as the simple cases seen in *icterus epidemius* bear to the fatal; a separation perhaps due to the amount of poison taken in either case.

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[*] Liebermeister, *Beiträge zur path. Anat. u. Klinik der Leberkrankheiten*, Tübingen, 1864, p. 185.

[†] Horaczek, *Die gallige Dyscrasie*, Wien, 1843, p. 93.

[‡] Leyden, *Beiträge zur Path. des Icterus*, Berlin, 1866, p. 131.

CHAPTER XXVI.

ICTERUS FEBRILIS.

IT was noticed more than two thousand years ago by Hippocrates that fevers are sometimes complicated by jaundice. Indeed it is chiefly as a complication of fever that the early writers speak of jaundice. If the jaundice showed itself before the seventh day it was a bad sign. If on the seventh, ninth, eleventh, or fourteenth, it was good, if the hypochondrium be not hard.[*] Sydenham noted the appearance of jaundice in the decline of the continued fevers of 1673-75.[†]

The jaundice has been thought by some to be due to a change in the blood. Dr. Murchison would appear to favour the belief that the jaundice is the result of an imperfect oxygenation or metamorphosis:[‡] Leyden, to some solution of the corpuscles themselves, at least in cases of pyæmia.[§]

Rendu has attempted, in much the same manner, to explain the jaundice of fevers by Gubler's theory of hæmapheism. In pneumonia, intermittent and yellow fevers, and pyrexia of all kinds, it is not the liver primarily affected; it is the blood. Under the influence of the fever and the poison of the disorder, there is an excessive destruction of blood corpuscles, greatly exceeding the physiological limits. Thus there is thrown into the circulation a large amount of pigment, in excess of that which the liver can use for the formation of bile, and which pigment the kidneys undertake to get rid of under the form of high coloured urine.[*] If, however, the fæces be found colourless, this theory will fall, but I cannot find that Gubler or his disciples have paid much attention to them.

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[*] Hippocrates, *Aphorisms*, iv. §§ 62 and 65, Littré's edition, t. iv. p. 524.

[†] Sydenham, *Obs. med.* ii. 13 in *Op. omnia*, ed. Greenhill, p. 211.

[‡] Murchison, *Clinical Lectures on Diseases of the Liver*, London, 1877, Sec. ed. pp. 395 and 411.

[§] Leyden, *Beiträge zur Path. des Icterus*, Berlin, 1866, p. 12.

Liebermeister, because he finds the bile of the gall-bladder thin and bright, thinks that the secretion is decreased, but that there is no hindrance to the flow of bile into the intestine, as the fæces are well coloured.[†] I fear I cannot endorse these statements. In the first place, the characters of the bile in the gall bladder correspond but little to those of the bile secreted by the liver, as the bile undergoes many changes by its sojourn in the gall-bladder; and in the second place I cannot agree with the statement that fæces are always coloured; in many cases which I have examined after death I have found the fæces colourless, and the duct free from colour close to the duodenum. My own opinion is is that the jaundice is in all cases caused by obstruction. The process in the stomach and duodenum, seen in high temperatures, spreads to the bile duct or its orifice. The mucous lining of the duct becomes swollen. A hindrance is thus offered to the flow of bile into the bowel. This hindrance may be complete or incomplete. The smallest provocation only is needed to cause the bile to enter the blood, and thus jaundice may be seen, while yet a certain quantity of bile is found in the intestines. This would explain the occasional presence of bile in the stools.

There is another cause of jaundice which must not be lost sight of. It is dependent on the parenchymatous changes always seen in high temperature. Cornil has shown, in all cases of parenchymatous degeneration of the liver, that the interlobular gall ducts are filled up with epithelium which is not present in the natural state. This state was found in all fevers, smallpox, and puerperal fever. It is not necessary for jaundice to show itself that these appearances be found everywhere in the liver.[*] This cause of jaundice is allied to the cause of jaundice in *icterus gravis*, and is to be relied on when the same severe symptoms, that are seen in *icterus gravis*, appear in the course of a febrile disorder attended with fever, a phænomenon which has now and then been noted.

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[*] Rendu, *Dictionnaire encyclopédique des Sciences méd.* Article Foie (pathologie) t. ii. p. 681. Cf. Dreyfus-Brisac, *De l'ictère hèmaphèique*, Paris, 1878, p. 60. A large number of observations, in which scarcely anything is said about the state of the stools.

[†] Liebermeister, in Ziemssen's *Handb. d. spec. Path. u. Ther.* Leipzig, 1874, Bd. ii. Theil i. p. 167.

Prussak has seen that in cases of jaundice attended by fever, the urine will sometimes give no reaction with Gmelin's test, or else a very imperfect one.[†] This should be borne in mind, as naturally much stress will be laid on the absence of bile pigment by the defenders of a hæmatogenous jaundice.

Körner has devoted a long series of articles to the consideration of *icterus febrilis* from a clinical point of view.[‡] He seems to think that a peculiar character is stamped on the disease by the presence of the jaundice, and differs greatly in his opinions from the conclusions to which other observers have been led. He says the fever is in most cases very severe, the rise of temperature being marked, with a redness and turgidity of the soft parts. There are special functional derangements of the organs of respiration and circulation; special changes in the stomach and intestines, to which nervous symptoms in some cases are added. There is likewise great muscular weakness. Upon all of these points Körner dilates with much minuteness of detail. The lungs give a clearer sound to percussion, the respiratory sounds are very variable, sometimes altogether absent; the heart is larger, and there is an interval between the systole and the pulse at the wrist. The second pulmonary sound is often accentuated: sometimes there is a systolic murmur audible. The arteries are dilated by the impulse of the heart more slowly, and a sort of vibration may be left at the acme of the pulse; there is also a murmur to be heard in the arteries.

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[*] Cornil, *Compte rendu des séances de la société de Biologie*, 1875, p. 306.

[†] Prussak, *Centralblatt f. d. med. Wiss.* 1867. p. 97. See p. 281 of this work.

[‡] Körner, *Allgem. Wiener med. Zeitung*, 1871, p. 105, No. 14-No. 22.

The liver and spleen are almost always enlarged.

The urine is decreased in quantity, and contains much urea, uric acid, and colouring matter, although but few chlorides. There is sometimes only a trace of bile pigment and albumen; but it is not the amount of albumen but its presence which is important.

All these appearances are due to changes in the nutrition from disturbances in the circulation. These are caused by the original disorder, and are owing to a decrease of the arterial pressure with an increase of the venous, from a weakening of the heart and contractile power of the arteries. It is in this way that jaundice is brought about, as the bile ducts are open. Körner thinks the plug of mucus may be a consequence of the jaundice, not a cause.

i. Pneumonia is not uncommonly complicated by jaundice, and is thence by certain Germans ill-named *pneumonia biliosa*.* It is thought by some to be often seen, by others rare; for example, Fismer, gives 5·5 *per*

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* It is sometimes said that this expression was invented by Maximilian Stoll. It is indeed used by him, but in quite a different sense. "Peripneumonia aut pleuro-peripneumonia, quam *Tissotus* biliosam seu putridam appellat." (*Ratio medendi*, Viennæ, 1789, Pars v. p. 85.) By bilious pneumonia Stoll evidently means what we to day called typhoid or asthenic pneumonia. For an excellent account of this see my friend Professor Leichtenstern's *Ueber asthenische Pneumonien*, in Volkmann's *Sammlung*, Innere Medicin, Leipzig, 1870-75, p. 633. How incorrect it is to call a disease complicated with jaundice "bilious" from this symptom only, may be seen in the last chapter of this work, that on Bilious Diseases.

cent. of 128 cases at Basel from the year 1863 to 1866; while in his own cases, which were carefully taken, the percentage was 28·3, out of 230 patients,[*] so that it is likely that the difference is due to want of notice being taken of slight changes.

It is considered doubtful if the presence of jaundice have any influence on the prognosis, while others think that its gravity is much heightened. Leyden believes that the bile acids in the blood do harm by their action on the blood corpuscles and on the heart.[†] In this, however, I scarcely agree, for it is not the jaundice itself which is so harmful as the cause of the jaundice, and the prognosis should be influenced by the evidence of the deep changes in the organs, albuminuria, delirium and the like, or by the signs of a severe gastric catarrh, so common in these cases; and still more by the type of the disease, if asthenic or sthenic. Out of Fismer's 65 cases of pneumonia complicated by jaundice 13 died, that is, 20 *per cent.* There were 230 patients in all, and of these 60 died; that is, 26·1. *per cent.*[‡] If we judge by these figures, the presence of jaundice seems to be rather favourable than otherwise. Mosler, however, found that 11 out of his 15 cases died, a mortality of 73 *per cent.*[§] but Mosler's cases seem from the first to have been bilious, that is, adynamic, pneumonia; and the presence of the jaundice was due in the fatal cases examined, to a catarrh of the duodenum extending to the bile ducts. The jaundice may be looked upon as an accident of the intestinal catarrh.

The relation of jaundice to pneumonia was formerly explained by the fact that pneumonia is more common at the right base than at the left, and that, the diaphragm being rendered motionless, no pressure could be exerted on the liver, and thus no bile driven out. This, however, hardly needs a serious consideration, for the jaundice ought only to arise in pneumonia of the right base. Another theory, that the jaundice is due to an increase of the venous blood pressure in the liver, and compression of the gall ducts, is supported by so good an observer as Jürgensen,* yet this can scarcely be allowed, for in extreme cases of hepatic congestion, such as heart-disease and emphysema, the jaundice is very slight, and often appears only late in the disease; the venous pressure in the liver must be great, long before the appearance of the jaundice.

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[*] Fismer, *Deutsches Arch. f. klin. Med.* 1873, Bd. xi. pp. 413 and 417.

[†] Leyden, *Beiträge zur Path. d. Icterus*, Berlin, 1866, p. 137. In this opinion Oppolzer shares. (*Allg. Wien. Med. Zeitung*, 1869, p. 12.)

[‡] Fismer, *loc. cit.* pp. 399 and 421.

[§] Mosler, *Deutsches Arch. f. klin. Med.* 1872, Bd. x. p. 279. Traube notes the common appearance of stupor, a grave symptom in "bilious pneumonia." (*Ges. Abh.* Berlin, 1871, Bd. ii. p. 692.)

In the greater number of cases which I have myself examined, I have found that there was some impediment to the flow of the bile into the duodenum; an obstruction sometimes so small that even the moving of the body after death was enough to overcome it, and allow the bile to pass into the duodenum. I have found all the rest of the intestine free from bile staining, and the fæces colourless, while the ducts, and the mucous membrane of the duodenum just outside the papilla, were deeply bile stained. In other cases I have found the duodenal portion of the duct free from colour.

It is possible that if the fever be severe, the jaundice may likewise be due to the parenchymatous changes which take place in the liver.

Dr. Cheadle noticed in a girl, aged six and a half years, that a jaundice rapidly disappeared during a pneumonia of the left upper lobe, and, after the pneumonia had run its course, the jaundice returned again, and was only cured when some weeks had passed. Dr.

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* Jürgensen, Ziemssen's *Handb. d. spec. Path. u. Ther.* Leipzig, 1874, Bd. v. Heft ii. p. 116.

Cheadle explains this by supposing that the bile pigments are burnt off in the blood by the fever; this is the more likely because during fever no more sugar is formed in the liver, and so an important combustible body is brought into the circulation at a time when the oxydation is at its highest. Thus bodies are brought to the liver which are already fully oxydised, and unfitted for making bile, and so but little bile pigment is brought into the circulation.[*]

ii. Typhoid fever is but rarely complicated by jaundice. I do not remember to have seen a case; and Sir William Jenner said in 1853 that he had never met with jaundice either in typhus or typhoid.[†] Dr. Murchison met with four cases at the London Fever Hospital, of which three were fatal.[‡] Abroad the proportion of cases seems higher: Griesinger says it is very rare, and always due to catarrh of the bile duct.[§] C. E. E. Hoffmann, in his very careful observations made at Basel, found that a slight degree of jaundice at the beginning was not so uncommon; but that well marked jaundice was rare, and seen later on in the disease. Of Hoffmann's 250 fatal cases, 10 were jaundiced; and he notes, as important for the pathology of the disease, that in all cases the degeneration of the liver cells was very advanced.[¶] Hoffmann likewise found the cylindrical epithelium of the gall ducts filled with fatty granules, indistinct in outline, and at last complete destruction. The larger ducts sometimes showed a catarrhal swelling.*

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[*] Cheadle, *British Med. Journal*, 1868, Vol. ii. p. 337.

[†] William Jenner, Gulstonian Lectures on Acute Specific Diseases, in *Medical Times*, 1853, March 26, p. 312. It does not appear among the list of complications observed by Nordt, (Virchow and Hirsch's *Jahresb. f.* 1876, Bd. ii. p. 24.) of 84 cases, or by Stricker in 88, (*Charité-Annalen*, 1876, p. 292) treated at the Charité in Berlin in 1875.

[‡] Murchison, *Clinical Lectures on Diseases of the Liver*, Lond. 1877, p. 401.

[§] Griesinger, *Infectionskrankheiten*, in Virchow's *Handbuch d. spec. Path. u. Ther.* Erlangen, 1857, p. 150.

[¶] C. E. E. Hoffmann, *Untersuchungen ueber die path. anat. Veränderungen d. Organe beim Abdominaltyphus*, Leipzig, 1869, p. 220.

The jaundice commonly appears late in the disease, sometimes after the fever has ended. It may, however, be seen in the first or second weeks.

The appearance of jaundice in typhoid must be looked upon as an unfavourable complication of the disease. For if it be due in most cases to the degeneration of the liver, as C. E. E. Hoffmann's observations would seem to show, it is evidence, especially if joined to albuminuria, of the wide-spread change which has taken place in the body, and which must be injurious to the patient's chances of recovery. In the earlier stages of the disease, the jaundice is probably due to the swelling of the mucous membrane of the gall ducts, of which C. E. E. Hoffmann has given anatomical proof.

Amongst the cases scattered through medical literature there is one worthy of being noted on account of the appearances seen after death and the name given to them. A boy, aged 9, was admitted into the Bristol Hospital, under the care of Dr. Burder, on May 26th, having been ill for five days before, with rigors: yellowness was apparent on admission. The disease was thought to be typhoid. The boy died on June 7th. The accounts of the examination are very meagre, but it is said there were jaundice, and general peritonitis with ulceration of the cœcum, as well as of the small intestine, and that the liver appeared to be a mass of small abscesses.† Abscess of the liver, and ulcerations of the large intestine are both rare in typhoid fever, in fact many might be disposed to deny the name of typhoid to a disease with these appearances.‡

iii. During the first or second paroxysms of relapsing fever, there is not uncommonly developed a jaundice, more or less severe. The percentage of cases attacked varies with the epidemic. Thus in the early Scotch and Irish epidemics, the presence of jaundice was so common that the disease was thought to be a mild form of yellow fever.[*] Sir William Jenner, in an epidemic in London, found only one-fourth jaundiced.[†]

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* Hoffmann, *op. cit.* pp. 216 and 222.

† Elliot, *Lancet*, 1874, vol. ii. p. 552.

‡ Cf. Samuel West, *Saint Bartholomew's Hospital Reports*, 1877, Vol. xiii. p. 215.

Dr. Tennent found that, out of 352 cases of relapsing fever treated at the Glasgow Fever Hospital, only 30 were at all jaundiced, and only 7 of these markedly so. If the jaundice were marked, the stools were of a light yellow, occasionally they were almost white. The jaundice appeared to have had no influence on the course of the disease, beyond somewhat lengthening it.[‡]

Lebert in Breslau saw very few cases in the epidemic of 1868, more in the winter of 1872-73, and most of all in the small epidemic of 1869. It is commonly but little marked, and soon disappears; but in some other cases the symptoms are more severe, the jaundice lasts longer, and is more intense, the patients become very weak, there is bilious vomiting, and the stools become colourless, so that Lebert says the cases resemble those of "bilious typhoid."[§] The appearance of jaundice makes the prognosis less favourable than in the uncomplicated cases.

The cause of the jaundice is probably, in the slight cases, a plugging of the ducts; of which Haenisch has given anatomical proof:[‖] in the severer, parenchymatous changes in the liver. Sir William Jenner thought it due to a functional disorder of the liver; bile is present in the urine he says, and the stools contain abundance of bile, and if death occur, the gall bladder is found full of bile, and the cystic and common ducts pervious.[*]

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[*] John Rose Cormack, *Natural History, Pathology, and Treatment of the Epidemic Fever in Edinburgh*, London, 1843, p. 22.

[†] Quoted by Griesinger, *Infectionskrankheiten*, in Virchow's *Handb. d. sp. Path. u. Ther.* Erlangen, 1857, p. 208. Nothing to this effect is said in the short passage which deals with relapsing fever in the Gulstonian Lectures.

[‡] Tennent, *Glasgow Medical Journal*, 1871, Vol. iii, p. 374.

[§] Lebert, Ziemssen's *Handb. d. spec. Path. u. Ther.* Leipzig, 1874, Bd. ii. Theil i. p. 281.

[‖] Haenisch, *Deutsches Arch. f. klin. Med.* 1875, Bd. xv. p. 65. There was one fatal case, complicated with pneumonia, of the four cases with jaundice seen in the epidemics of relapsing fever at Griefswald from 1868 to 1873. The ducts were found plugged with mucus.

The gall bladder being found distended would rather be an argument in favour of an obstruction to the flow of bile than otherwise. Dr. Murchison thinks the slighter cases due to "congestion of the liver"; the severer, to the imperfect metamorphoses.[†] I prefer myself to attribute the cause to one which can be detected after death, as F. Herrmann in the epidemic at St. Petersburg found in his cases a fatty infiltration of the liver cells, filling of the gall bladder, a catarrhal swelling of the gall ducts, and a granular appearance of the striated muscles, together with loss of colour in the fæces.[‡]

iv. Jaundice in typhus is but rarely seen. It has been stated by some authors[§] that in certain epidemics, jaundice was exceedingly common, and recalled the disease known as "bilious typhoid." It seems, however, probable that epidemics of relapsing fever have been taken for typhus. Sir W. Jenner, as stated before, had in 1853 never seen a case of typhus complicated with jaundice.[‖] Dr. Murchison says that out of 7,604 cases of true typhus admitted into the London Fever Hospital in four years, jaundice was noted in 16; that is, one in every 475 cases. Out of these 16, 12 were fatal. Dr. Murchison thinks the jaundice due to the same cause as in acute yellow atrophy, for the appearance of the liver seen after death closely resembles this disease.[*] Frerichs believes the jaundice to be due to the same cause as in pyæmia.[†]

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[*] Jenner, Gulstonian Lectures on the Acute Specific Diseases, in the *Med. Times*, 1853, March 26, p. 312.

[†] Murchison, *op. cit.* p. 398.

[‡] F. Herrmann, *St. Petersburger med. Zeitschrift*, 1867, Bd. xii. p. 7.

[§] Frerichs, *Klinik d. Leberkrankheiten*, Braunschweig, 1858, Bd. i. p. 174.

[‖] Jenner, *loc. cit.* Out of 1858 cases of typhus seen by Herrmann at St. Petersburg in 1874 there does not appear to have been a single case of jaundice. (*St. Petersburger med. Wochenschrift*, 1876, No. 16.)

v. Notices of the appearance of jaundice in scarlet fever are scattered in medical literature,[‡] but there was no good account of this complication until Dr. Murchison described it. He believes the appearance of jaundice in scarlet fever to be extremely rare. He found it in only 5 out of 2000 cases. Three of the five cases were fatal. Two of these were examined after death, and it was found that the liver was pale and fatty in one, and nutmeg in the other. In both the bile ducts were patent, and the urine albuminous.[§] The jaundice would thus probably be due to the parenchymatous change in the liver. Dr. Gee tells me that, in a fatal case, he found the lymphatic glands in the porta of the liver much enlarged, and pressing on the gall ducts. To this pressure he attributes, in this particular case, the symptom of jaundice. Danielssen has published a fatal case of jaundice after scarlet fever. The patient, 20 years of age, a young woman, was thought to be cured, when death overtook her the sixth day after the apperrance of the eruption. There was found a rapidly developed fatty change in the liver, spleen, kidneys, and heart, with ecchymoses of the lungs and kidneys, just as in phosphorus poisoning.[‖] Dr. Thomas Barlow has observed a case in which cirrhosis of the liver followed scarlet fever.*

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[*] Murchison, *op. cit.* p. 399.

[†] Frerichs, *loc. cit.*

[‡] Graves, *Clinical Lectures*, Dublin, 1864, p. 344. George Harley, *Jaundice*, London, 1863, p. 93. Budd, *On Diseases of the Liver*, London, 1857, p. 169. McSwiney, *Dublin Quart. Journ. of Med. Science*, 1870, Vol. xlix. p. 454. There is no case mentioned among the epidemics of scarlet fever at Würzburg spoken of by Voit. (*Jahrb. f. Kinderheilkunde*, 1872, Bd. v. p. 255.)

[§] Murchison, *op. cit.* p. 402.

[‖] Danielssen, *Bericht ueber die Wirksamkeit des Lungegaards-spitals im Triennium* 1865-67, Christiania. Abstract in Virchow and Hirsch's *Jahresb. f.* 1868, Bd. ii. p. 255, but most meagre.

Kersch has noted the case of a little girl aged 3, in whom the jaundice appeared the 7th day after the eruption, which was then beginning to disappear. The stools were colourless, the urine high coloured. Dropsy came on, but the child recovered so far as to cease to receive medical attendance about six weeks after first falling ill.†

The following notes are those of a case of scarlet fever complicated with jaundice, and probably also with further disease of the viscera, which came lately under my notice. I am indebted for them to Mr. Joseph Armitage, of New College, Oxford.

John Keelin, aged 14, admitted into Radcliffe ward, Nov. 14th, 1879, under the care of Dr. Gee. He has been in Henry ward for hip disease. The disease is of old standing, and is accompanied by albuminuria. He is said to have felt unwell on Nov. 12th: on the morning of Nov. 14th, scarlet rash, and sore throat were noticed, and he was removed to Radcliffe. 10 p.m. temp. 103·2. F.

Nov. 15th. 10 a.m. temp. 102·8 F. restless night: slight rash on shoulders. Tongue dry and red. Bowels open. Urine five-sixths of albumen, sp. gr. 1026.

Nov. 16th. Bad night, but not so feverish: dusty red punctiform rash on chest and arms. Throat slightly inflamed. Urine as before.

Nov. 17th. Good night. Tongue dry and red: papillæ slightly enlarged. Takes food well. Bowels open several times, loose motions of a natural colour. Urine noticed to be dark: on adding fuming nitric acid to the dark urine, it became of a dark grass green colour, albumen five-sixths, sp. gr. 1024.

Nov. 18th. Distinctly, but slightly, jaundiced this morning. Great tenderness over the liver. Liver can be felt for about three-quarters of an inch below the ribs in the nipple line. Urine as before. Bowels open several times.

Nov. 20th. Still slightly jaundiced. Skin beginning to peel. Urine as before. Nurse reports stools to be white.

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* Thomas Barlow, *Trans. of the Pathological Society of London*, 1877, Vol. xxviii. p. 355.

† Kersch, *Memorabilien*, 1878. Jahrg. xxiii. p. 209.

Nov. 22nd. Still jaundiced. Bowels open several times. Loose motions. Urine as before.

Nov. 25th. The jaundiced tint has disappeared, but the urine remains dark.

Nov. 28th. Urine still appears dark, but does not turn green on adding nitric acid. Albumen five-sixths, sp. gr. 1026. Skin peeling rapidly.

Dec. 1st. The boy remains very weak and has constant diarrhœa: his evening temperature is always above the normal, generally about 100·5, his morning temperature normal or nearly so. All traces of bile have disappeared from the urine, which remains highly albuminous: the liver is slightly enlarged: the spleen is not palpable. His skin is still peeling.

He made a very slow recovery.

vi. Jaundice is sometimes seen complicating fevers due to malaria. Owing to the improved drainage and tilling of the land, agues are but seldom seen in London, save among the lower classes of the population, and not commonly among them ; or they are seen in those who have received the germs of the disease in foreign parts.

In our northern climates jaundice but seldom complicates ague. I have heard indeed of a case in a gentleman who took the infection at Aigues Mortes. in the South of France, and in whom the disease and the complication appeared after his return to London. The cachexia caused by malaria must not be confounded with jaundice. The state of the conjunctivæ and urine will decide this.

Ritter, who has had great experience in the malarious disorders of the north, says that in 1869, he met with jaundice complicated with ague no less than five times. Ritter thinks it dependent on the extreme disorder of the mucous membrane of the intestines which was very common at that time. The gall bladder could be felt, the liver preserved its natural size, and the fæces were not completely colourless. The jaundice was never severe, and all the cases quickly recovered. Ritter believes it to be a jaundice from retention, some temporary obstruction to the ducts arising from the duodenum. One case recorded by Ritter is curious. A man aged 43 had, about 20 years before he came under observation, an attack of melancholia which lasted for six months. He had three attacks of a tertian ague, with jaundice and a tender gall bladder. The fever disappeared with quinine. In 8 days the jaundice was very intense, and the stools completely colourless. Five nights were passed without sleep, and the patient fell more and more into the old melancholy, and even made attempts on his life. After 10 days the jaundice disappeared, and with it the melancholy.*

Léon Colin, who had the opportunity of studying the the phænomena of malarial fever in the French army of occupation at Rome, says that jaundice is seen at the decline of remittent fever. It is specially in the gastric forms that it is noticed. The yellow colour comes on as the congestion goes off; the conjunctiva shows the colour very plainly. The jaundice sometimes appears very suddenly; for example, a patient may be left over night with a high temperature and a red skin, and the next morning he is found free from fever, but jaundiced. During the summer and autumn, the complication is seen much more often. Colin says that in July 1864 he had only a proportion of 1 to 20; that is, one case of jaundice to 20 of the gastric form. In the last week of August, however, the ratio had risen, and was as 1 to 4. In September, the remittent fevers are almost always attended by jaundice, and it is with this form that old sufferers from malaria are chiefly attacked.†

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* Ritter, *Arch. f. path. Anat.* 1870, Bd. l. p. 169.

† Léon Colin, *Traité des Fièvres intermittentes*, Paris, 1870, p. 163. Boudin is often quoted to show that in warm climates, such as Algeria, malarious fevers are often attended by jaundice, even in seven-tenths of the cases. I cannot think that the authors who so quote Boudin can have read what he says. "Suivant

The prognosis in these simpler cases does not seem to be made any worse by the appearance of a jaundice.

The cause of the jaundice is uncertain. It is probable, as Ritter suggests, that the jaundice is due to an obstruction; but it must not be too hastily assumed, as Hertz* does, that the jaundice is due to a gastro-intestinal catarrh, for, however likely this may be, there is of it at present no anatomical proof. Colin has fallen back on the old notion of a polycholia because there is abundance of bile, he says, in the stools and vomit.†

There is a curious disorder, clearly allied to the malarial fevers, which the French have named *fièvre bilieuse hématurique*, or *hémorrhagique*, or *mélanurique*, from the deep red colour or blackness of the urine. It seems to be a disorder *sui generis*, and is not to be confounded with the yellow fever, with which it was once thought to be identical. The first attempt at a complete description of the disease was made by Barthélemy-Benoit,‡ and the greater part of the literature of the subject has been supplied by the medical staff of the French Navy stationed at Senegal, Guadaloupe, and other tropical colonies. Bérenger Féraud has published a monograph on the subject.§

The disease is only seen in those who have suffered many attacks of malarial fever. The onset of the disease is marked by two attacks, sometimes only one attack, just like those of the ague, but longer and severer than those to which the patient is used. The second attack follows the first in 48 hours, and is

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M. Nepple, la forme gastrique s'attache aux *trois quarts des fièvres* de la Bresse marécageuse. En Afrique, je l'ai recontrée chez les *sept dixièmes* des maladies." (*Traité des fièvres intermittentes*, Paris, 1842, p. 318.) "Bilious" with Boudin has the same value as with Stoll, and is equivalent to gastric.

* Hertz, *Malarial Diseases*, in Ziemssen's *Handbook*, American ed. Vol. ii. pp. 636 and 643.

† Colin, *loc. cit.*

‡ Barthélemy-Benoit, *Archives de méd. navale*, 1865, t. iv. p. 4.

§ Bérenger Féraud, *De la fièvre bilieuse mélanurique*, Paris, 1874.

severer than the first. In some cases the vomit may already be green, and deeper in colour than natural. This is the stage of *prodroma*, in which what is about to happen to the patient can hardly be foretold. Bérenger Féraud divides the cases, according to the symptoms which develope, into four classes: i. the slight or intermittent cases: ii. the cases of medium gravity: iii. the serious or grave cases: iv. the cases of great severity.*

In the mild cases, the specific attack begins as a rule 24 hours after the beginning of the last aguish attack, sometimes later, even 48 hours. There are violent shiverings, frontal headache, and painful sense of distension of the right hypochondrium. It is at the onset of this attack that the jaundice, as well as the black urine, is seen. The black urine makes its appearance with great suddenness. Before the onset, the patient makes water of natural colour, but the next time it shows the peculiar darkness. The colour varies from a clear maroon to a colour almost black, like port-wine or black coffee. There is often a thick deposit, grey or deeper in colour than the rest of the urine. With the end of the attack, the urine regains its natural appearance.

During the attack there is great nausea and vomiting; and the vomited matters have a peculiarly fine green appearance; they are quite limpid and contain no lumps or particles, unless of course food, or other foreign matter, have been introduced into the stomach.

There are rarely more than two attacks, and if the patient have taken and absorbed enough quinine, convalescence ought to be established by the fifth or sixth day, and health restored at the end of three weeks or a month.

In the second degree of the fever, that of medium severity, the attack begins by a long and intense fit of shivering. The patient himself is alarmed. The headache is general, the face pale, before it become jaundiced; the jaundice slight or well-marked, abundant and frequent vomiting of a green matter which contains solid matter like chopped spinach. There is great thirst, but drink always brings on renewed vomiting. There is an abundant diarrhœa, the stools being liquid and of a brown-red or black colour. The intestinal evacuation closely resembles the urine passed at the same time, and the two have been mistaken for each other. The urine is of the same colour as in the milder form, but it is often turbid at the moment that it is passed. During the remission, the urine clears somewhat, but not altogether. The spleen and the liver become large and painful. There is much pain in the loins: these three last symptoms being due, in the opinion of the French writers, to congestion of the liver, spleen, and kidney.

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* Bérenger Féraud, *op. cit.* p. 117.

The reaction from this state comes on slowly, after one to three hours. The attack itself lasts from six to eight hours. There is usually but a short remission, scarcely to be called an intermission, of the fever, and a fresh attack equally severe with the foregoing comes on. The attacks become more irregular, and the remissions shorter, as the disease lasts. The febrile stage lasts from 5 to 7 days.

If the patient be about to recover, the remissions become longer, the jaundice disappears slowly, and the urine is clear, and free from the dark tint. An epistaxis is sometimes seen as convalescence comes on; it weakens the patient, but is otherwise not of evil augury. Should the jaundice become stationary, or increase during the convalescence, it is a sign of a coming relapse. The convalescence is often long, five or six weeks.

In the third degree of the fever, that of great severity, all the symptoms described under the second degree are present, but are much more intense; the prostration of the patient is very great, the vomitings are incessant, the thirst intense, while the least attempt to quench it brings on the vomitings afresh. The vomited matter is green, as described above. To the vomitings is sometimes joined a hiccup most distressing to the patient, and to the bystanders. Bérenger Féraud relates a case in which this hiccup was so loud and distressing to the other inhabitants of the ward, that the patient had to be placed by himself. It is of bad omen. There is great tenderness of the belly, which the hiccup and vomiting increase. There is often complete sleeplessness, and epistaxis may come on, adding much to the gravity of the case.

Towards the end, the pulse sinks and becomes compressible, the jaundice becomes less, and may even disappear, and the patient dies from asthenia, or a sort of asphyxia.

In the cases of recovery, the fever lasts from 7 to 10 days, sometimes in two divisions; the convalescence lasts between 45 and 65 days. In the fatal cases, death may take place from the 5th to the 30th day; the mean is the 12th day.

In the fourth form, which Bérenger Féraud calls "*sidérante*," death takes place rapidly, during the first attack, which is very rare in the other forms of the disease. It is seen only in those whose health has been shattered by many attacks of malarious fever. The attack begins with all the symptoms common to the other forms, but they are infinitely more severe: the green vomitings, the hiccup, the diarrhœa, are all terrible to witness. There is at first passed a little black urine, but after, the patient passes none at all, and there may be an almost complete anuria for 24 or 48 hours. The disease lasts from 2 to 5 days, ending in death; the mean is about 3½ days.

On examination after death, the body is found to be universally jaundiced. There are said to be no petechiæ or ecchymoses as in yellow fever; and the *rigor mortis* is well-marked. There is nothing of importance found in the head or chest;* but all the noteworthy appearances are found in the belly. There is no *vomito negro* found in the stomach. The mucous membrane is found softened and reddened, an appearance which Bérenger Féraud attributes not to the febrile disorder, but to alcohol, the abuse of which is universal in Senegal.†

If the patient die early in the disease, the liver is found increased in size, in weight, and in consistence. It is, however, more friable, although more resistant. The ordinary red colour is much deepened, in some spots deeper than elsewhere. The bloodvessels are said to be full of blood, and blood drops from the cut surface. If the patient have died after the fifteenth or twentieth day, it is said that the liver is pale, and very little blood escapes on section, but the size, weight, and consistence of the liver are said to be the same as in the earlier stage.

The gall bladder is usually distended with bile; the gall ducts are said by Pellarin to be empty, and stained by a pale yellow fluid bile.‡

The spleen is always enlarged and may weigh as much as 1700 grammes or 3½lb. Its consistence is very variable, being sometimes firm, at other times diffluent.

The kidneys are also greatly increased in weight, from 200 to 300 grammes. They are jaundiced like the other organs, but their tissue is of a deep red brown. It shows numerous ecchymoses, which may be as small as a hemp-seed, or take up four fifths of the organ. These ecchymoses are chiefly seen in the cortex, but they may extend into the medulla. Sometimes nothing can be seen in the kidney but a mass of blood clot.

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* The heart fibres are said by Dr. Joseph Jones to be free from oil. (*New York Med. Record*, 1873, p. 417.)

† Bérenger Féraud, *op. cit.* p. 73.

‡ Pellarin, *Archives de méd. navale*, 1876, t. xxv. p. 326.

The microscope and chemical analysis have not as yet thrown much light upon this disease, although there are many points which might be cleared up by careful hands accustomed to the use of these two methods. For instance, the state of the urine and the cause of its black colour during the attack. There seems to be no doubt that the urine contains a large proportion of albumen, and, the earliest observers thought, blood also. Red blood corpuscles were found, though with some difficulty, by Hugoulin and Borie,[*] and Pellarin.[†] Bérenger Féraud, on the other hand, never was able to detect a single corpuscle,[‡] and asserts that the black colour is entirely due to the presence of a large quantity of bile in the urine, bile acids and bile pigments. He says that his observations were confirmed by Bouchardat, who analysed some of the urine sent to him from abroad. Other observers deny that the bile pigments can be found, and think the colour due to blood or its chemical constituents. I think it probable from the evidence, though it is by no means shown, that the colour is due to hæmoglobin, or some derivative of hæmoglobin. Legrand once found Heller's test for blood to succeed;[§] the hæmorrhage into the kidney and the large quantity of albumen, make it likely that the colour of the urine is due to blood, which may be changed in some way. It is also likely that the bile pigments are present in the urine, perhaps masked by the large quantity of albumen and the colouring matter of the blood.

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[*] Hugoulin and Borie, reported by Barthélemy-Benoit, *Arch. de Méd. navale*, 1865, t. iv. p. 125.

[†] Pellarin, *ibid.* 1876, t. xxv. p. 307.

[‡] Bérenger Féraud, *op. cit.* p. 280.

[§] Legrand, reported by Pellarin, *op. cit.* p. 386.

Of that which in this treatise interests the reader most, the cause of the jaundice and the state of the liver, there exists almost less means for forming a sound opinion. There is but little addition to knowledge by asserting that the greater number of these cases are due to catarrh of the ducts.[*] Nor do I think the facts sufficient for asserting the jaundice, the green vomit, and the black urine to be due to a polycholia, or excessive secretion of bile by the liver. For, in the first place, although Bérenger Féraud has had the vomit analysed, and believes the colour to be due to biliverdin,[†] yet I scarcely think the evidence offered conclusive; and there may be more than one opinion as to the cause of the black colour of the urine.

For myself I am inclined to look for the cause of the jaundice in the liver itself. Histological examinations can scarcely be said to have been made. The increased consistence seems to me to be probably due to a cirrhosis, not an uncommon result of malaria; the hepatic cells are preserved, but are said to be full of fat and pigment granules;[‡] and Cuzent could find no sugar in a piece of liver sent to him by Pellarin.[§]

One of the very few things known for certain about this disease is that it is not yellow fever. This is shown by its attacking only old sufferers from malaria, by the absence of black vomit, and by the presence of black urine. There is also no such extensive fatty change found after death.

The treatment would seem to be conducted best by the exhibition of large doses of quinine persistently administered.

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[*] Hertz, *Malarial Diseases*, Ziemssen's *Handbook*, American Ed. Vol. ii. p. 643.

[†] Bérenger Féraud, *op. cit.* p. 286.

[‡] Barthélemy-Benoit, *op. cit.* p. 112. Pellarin, *op. cit.* p. 388. Joseph Jones, *loc. cit.*

[§] Cuzent, reported by Pellarin, *Arch. de méd. navale*, 1865, t. iii. p. 135.

vii. According to Frerichs, Marechal was the first to point out that in pyæmia the skin and conjunctiva were often yellow.[*] Bérard denied that this yellowness was a jaundice;[‡] but the statement has been abundantly disproved by Frerichs and others, who find that the blood, serous exudations, and urine, contain bile pigment.[§] There is no longer any doubt that the yellowness is a true jaundice.

In pyæmia the liver is but rarely found natural. Waldeyer found it free from disease in only 20 *per cent.* of all cases, and if the microscope were not always used, it is probable that the percentage would be higher, as cloudy swelling of the cells of the liver often exists, even when the liver itself has a perfectly normal appearance to the naked eye. This cloudy swelling of the cells was seen by Waldeyer in 30 *per cent.* of the cases. Joined to this there was "not seldom" seen an increase of the connective tissue in the portal tracts. Waldeyer found in all his cases of jaundice a well-marked plug of mucus in the intestinal portion of the bile ducts. In 6 *per cent.* of the cases there were abscesses in the liver.[‖]

Changes in the liver being thus so manifold and so common, it seems to me unnecessary, as some have done,[¶] to speak of a change in the blood. Leyden's grounds for believing that the jaundice is hæmatogenous are, apparently, the slight degree of the colour of the

[*] J. F. A. Marechal, *Recherches sur certaines altérations qui se developpent au sein des principaux viscères à la suite des blessures ou des opérations*, Thèse de Paris, 1828, p. 23. He notes grave disorders found in the liver, but does not think the yellowness due to these, but to the pus.

[†] Bérard, *Dictionnaire de Méd.* Paris, 1842, 2e éd. t. xxvi. p. 490. The urine and fæces, he says, do not offer the characters which they show in jaundice.

[§] Frerichs, *op. cit.* Bd. i. p. 169.

[‖] Waldeyer, *Arch. f. path. Anat.* 1867, Bd. xl. p. 408.

[¶] Leyden, *Beiträge zur Pathologie des Icterus*, Berlin, 1866, p. 11. Murchison, *Lectures on Diseases of the Liver*, Lond. 1877, p. 404.

skin and conjunctivæ, the slight reaction given by nitric acid, and the absence of the bile acids in the urine. As to the small amount of pigment, it should be borne in mind that in febrile jaundice, the reaction is often ill-marked. Dr. Murchison says there is plenty of bile in the motions; that after death the liver contains purulent deposits, or is pale and anæmic, and that the bile ducts are patent and free from inflammation. This author attributes the jaundice, as he does that seen in so many other forms of fever, to imperfect metamorphosis.

In the face of the evidence offered by Waldeyer as to the constant existence of a plug of mucus in the ducts of the jaundice of pyæmia, I think this must be accepted as the cause of the jaundice.* Even if a plug of mucus be not found, the parenchymatous degeneration of the liver offers a sufficiently good explanation of the phænomena, without invoking any far fetched theories which have no support from morbid anatomy.

Endocarditis may sometimes be attended by jaundice. Frerichs has recorded a case, apparently of *icterus gravis*, following acute rheumatism and endocarditis. Frerichs believes the jaundice due to pyæmia, some septic infection of the blood, and not to a plugging of the portal vein or hepatic artery. No temperatures are given, as the observation dates from 1856; but the liver was found large, pale, and flabby; the acini were not visible, and the cells, which were well preserved, were filled with granular masses, and also partly with fat drops.† In this case the jaundice seems certainly due to the parenchymatous degeneration of the liver, either from the fever, or some septic infection. It is probable that the same explanation awaits the cases of Lancereaux,[*] Charcot and Vulpian,[†] and Dujardin Beaumetz.[‡]

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* Säxinger (*Prag. med. Wochenschrift*, 1864, No. 34, quoted in Hueter, Die septik. und pyaem. Fieber in von Pitha u. Billroth's *Handbuch*) found a like catarrhal state in puerperal fever and jaundice.

† Frerichs, *op. cit.* Bd. i. p. 171.

Verneuil has attempted to establish a new variety of jaundice, an *icterus traumaticus*, which he again divides into two, the jaundice of pyæmia, and the simple jaundice of the wounded, which he says he has seen come on in persons suffering from slight surgical lesions. His first case appears to be an *icterus febrilis*, as it was preceded by shivering and the setting up of a sort of erysipelas. The two remaining cases are certainly not simple; one is a case of biliary colic, the other of cirrhosis.[§] Dupont has in like manner recorded a case of wound of the thigh, and erysipelas and jaundice setting in together. Although the temperature was sometimes over 40°C. yet the pulse never rose above 80, and was sometimes as low as 60.[‖]

viii. Acute rheumatism is sometimes complicated by jaundice. Graves says that he has seen this complication in eight or nine cases, and that it was followed by urticaria.[¶] Monneret is said by Chatard to have seen 15 cases of rheumatism and jaundice, accompanied by swelling of the liver, which state Monneret would appear to call rheumatism of the liver. Baillet has published ten of Monneret's cases in his thesis, and in some of these, the jaundiced state of the skin was noted 24 hours before the pains in the joints came on. Baillet thinks that there is a rheumatic affection of the fibrous capsule, and the fibrous tissue of the liver may be affected with rheumatism just like the fibrous tissue of the heart, brain and bladder. This view is taken by Chatard, who has noticed two new cases.* There is, however, no evidence brought forward either by Baillet or Chatard from morbid anatomy; and their views must be dismissed in favour of the opinion which ascribes to like causes the jaundice seen in all cases of febrile disorders.

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[*] Lancereaux, *Mémoires lus à la Société de Biologie*, 1862, p. 2.

[†] Charcot and Vulpian, *Gaz. méd.* 1862, p. 386.

[‡] Dujardin Beaumetz, reported by Jules de Roquetaillade, *étude sur la coexistence dans les états généraux graves de l'endocardite et de l'ictère*, Thèse de Paris, 1874, p. 7.

[§] Verneuil, *Bull. de l'acad. de méd.* 1872, p. 841.

[‖] Dupont, Virchow and Hirsch's *Jahresb. f.* 1876, Bd. ii. p. 511. Abstract from *Arch. méd. belges*, 1876, mai, p. 163.

[¶] Graves, *Clinical Lectures*; Neligan's ed. Dublin, 1864, p. 339.

There is a case published by Féréol of jaundice following an attack of acute rheumatism and ending in death. There was also a papular erythema which appeared about the same time as the jaundice. There was no examination after death, and the case is very obscure.†

Acute tuberculosis has been noted by Dr. Hilton Fagge to be complicated by jaundice.‡

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* Chatard, *Abeille méd.* 1863. Abstract in Canstatt's *Jahresb. f.* 1863. Bd. iv. p. 63.

† Féréol, *Gaz. hebd.* 1874, p. 769.

‡ Hilton Fagge, *Guy's Hospital Reports*, 1875, Vol. xx. Third series, p. 162.

CHAPTER XXVII.

ICTERUS SYPHILITICUS, ICTERUS A VENENIS.

THE charlatan Paracelsus is said to have noted the complication of syphilis with a jaundice, which could not be cured until the venereal disorder were overcome.*

Astruc rather hints at a cirrhosis as a consequence of syphilis than a simple jaundice, for he says that the "passage for the circulation is so stop'd up, that the Blood which should pass through the Vena Porta to the Liver, is forc'd to remain in the capillary origins of that Vein;" thence scirrhus, jaundice, piles, vomiting of blood, fluxus hepaticus.† Before this, however, he says: "the Jaundice, if the Bile being obstructed in its secretion shall abound in the Blood; yellow if the colour of the bile is yellow; black, if that be black."

Portal, after commenting on the old notion that syphilis had its chief seat in the liver (a notion which might well be entertained by those who held the physiology which prevailed before Harvey) speaks of the jaundice as one of the evils following on syphilis, and which could only be cured by the use of mercury.‡

Ricord noted two cases of jaundice complicated by syphilis;§ but to Gubler belongs the merit of having first pointed out that jaundice commonly comes on at the beginning of the secondary stage, and the relations of the jaundice to the general infective process.[*] Since that time, this complication of secondary syphilis has been noted by several writers.[†]

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* Paracelsus, quoted by Gruner, *Aphrodisiacus sive de lue Venerea*, Jenæ, 1789, p. 134. "Icterus cum morbo gallico copulatus non curatur nisi subacta materia venerea."

† Astruc, *Treatise of the Venereal Disease*, Book iv. Chapt. 5. § iii. 3. Barrowby's Translation, Lond. 1737, Vol. ii. p. 84, Cf. pp. 7 and 49.

‡ Portal, *Observations sur la nature et le traitement des maladies du foie*, Paris, 1813, p. 373.

§ Ricord, *Clin. icon.* Paris, 1851, Planche 18.

Gubler has collected 7 cases in which the jaundice followed a syphilitic infection; it accompanied the syphilitic exanthem, and was always preceded by digestive troubles, loss of appetite, nausea, bitter taste in the mouth, and pain at the epigastrium. These could not be set down to drunkenness, bad food, or mental emotion, for these were present in only one case. None was treated with mercury before the jaundice came on.

The jaundice may be slight, moderate, or severe. It rapidly attains its *maximum* of intensity. The length of time that it lasts varies much; sometimes very short, it might go on for a fortnight or more.[‡]

Gubler thinks that the jaundice is due to the syphilis for several reasons:

i. The absence of the common causes of jaundice. The presence of gastric troubles, noted by Gubler himself, may be by some looked upon as a common cause of jaundice.

ii. The coincidence with the syphilis. It may be objected that Gubler has, at the most, collected or observed only 8 cases, and that these are not large enough for any inference.

iii. The jaundice appears at the same moment as the syphilitic symptoms, at a determined moment of the general disease.

iv. The jaundice has a special character, and may be placed among the manifestations of the special diathesis.

v. Specific treatment cures the disorder.

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[*] Gubler, *Gaz. méd. de Paris*, 1854, p. 186.

[†] See Quinquaud, *Les affections du foie*, Paris, 1879, p. 94.

[‡] Gubler does not seem to have looked at the stools or tested the urine in any of his cases: a like inadvertence may be noted in his work on hæmatogenous jaundice.

There is no doubt a strong resemblance between the effects of the syphilitic virus and those of other poisons, organic and inorganic. Ricord is said to have compared it to the bite of a venomous animal,* and there is certainly much to justify the analogy. There are some cases of *icterus gravis* which have been set down to the action of the syphilitic virus, the fatal accidents happening within a few weeks or months of the infection. And if Gubler's views be correct, there is here another example of a poison in one person causing only a simple catarrh of the stomach and duodenum; in another, fatal jaundice from parenchymatous degenerations everywhere.

If Gubler's statement that all these cases of syphilitic jaundice are preceded by gastric troubles hold good in cases yet to be observed, the most probable cause of the jaundice will be a catarrh of the bile ducts, and no special lesion of the liver. Gubler, however, seems to think that there is some special syphilitic lesion of the liver at this stage, manifesting itself by the jaundice.

The treatment should be directed chiefly to the specific state, taking care not to aggravate the intestinal catarrh by the injudicious use of mercurials. Gubler thinks part of the proof that jaundice is due to syphilis is the rapidity with which the jaundice yields to anti-syphilitic measures. It should be remembered, however, that simple jaundice nearly always rapidly disappears, even without treatment.

ICTERUS A VENENIS.

It has long been known to physicians that the introduction of certain poisons into the body is apt to be followed by jaundice. Some of these have been discussed in a foregoing chapter. There now remain certain animal and vegetable poisons which, according to some writers, may cause jaundice. Mushrooms are specially accused of this; Lanzoni speaks of a countryman who became suddenly yellow, as much as jaundiced people are, after the eating of poisonous fungi.[*] Portal says that the acrid vegetable poisons, such as the celandine, spurge, clematis, and arum, cause the jaundice.[†] It is, however, the bites of animals that have been thought specially prone to be followed by jaundice. Some authors have said that the bites of even non-venomous animals, such as dogs and cats, may cause jaundice; the venomous snakes certainly seem to be able to cause jaundice, and of these the viper tribe more than the others.

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* Ricord, quoted by Gubler, *op. cit.* p. 278.

Amongst all the horrors of Africa described by Lucan, jaundice does not appear as one of the diseases brought on by the monsters of the desert.[‡] A hundred years or more after, a jaundice from the bites of vipers was spoken of by Galen. In discussing the question if jaundice ever arise without disease of the liver, he says that he has seen a jaundice come on from a change of the blood into bile[§] from some strange corruption, such as follows the bites of beasts. It happened that a slave of the imperial household, whose work it was to hunt out vipers, was bitten by one of these beasts. He took remedies for this; but becoming a leek-green colour, he was given a different drug, by means of which his jaundice was removed. Galen, it must be noted, attributes the jaundice in this case to a change in the blood. Paul[||] and Aëtius[¶] also both speak of a jaundice following the bites of venomous beasts.

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[*] Lanzoni, *Tract. de Venenis*, Cap. v. in *Op. Omn.* Lausannæ, 1738, t. i. p. 28.

[†] Portal, *Observations sur la nature et le traitement des maladies du foie*, Paris, 1813, p. 140.

[‡] Lucani, *Pharsalia*, Lib. ix. circa v. 600.

[§] Galen, *de locis affectis*, Lib. v. Cap. viii. ed. Kühn, Vol. viii. p. 355. "ὁρᾶται δὲ καὶ χωρὶς κρίσεως ἐκχολούμενον ἐνίοτε τὸ αἷμα."

[||] Paul of Aegina, Lib. iii. Cap. 50. Adams' Translation, Vol. i. p. 581.

[¶] Aëtius, *Tetrabibli tertiæ*, sermo ii. Basil. 1542, p. 582.

It must be owned that very little indeed is known about the jaundice that follows the bites of vipers. It is not even known if the stools be free from colour, although it has pleased Frerichs to state that the vomited matters and the fæces contain bile.[*] This statement appears to me to be explained by the fact that in many cases of snake-bite green matters are said to be vomited, but then jaundice is not spoken of as an accompaniment. Of the urine nothing is known.

The jaundice in many cases appears to be intense; Galen says his patient was of a leek-green colour; and Portal says that an apothecary, whom he knew, was bitten by a viper, and soon after became yellow all over his body: later on the jaundice became green, and on the third day it was almost black.[†]

Mead, in his essay on the poison of the viper, mentions the jaundice as a very extraordinary and surprising effect, and explains it by supposing that a constriction or nervous spasm may almost suddenly so straiten the orifices of the ducts into which the bile is to pass, that its derivation into them will be stopt.[‡]

Fontana takes a different view. Some authors, he says, think the jaundice due to the narrowing of the biliary pores as they arise from the substance of the liver; the secretion of bile is thus rendered impossible, and the bile accumulates in the blood. Fontana rejects this theory because the bile is not formed beforehand in the blood, but is made in the liver. Neither will he allow a spasmodic contraction of the ducts, for anatomy teaches us that the nerves are not irritable,* and that the ducts are not made of muscular fibres. The convulsions, which those bitten by vipers suffer, throw light upon the cause of the jaundice; the stomach and duodenum become narrowed, and the orifice of the gall ducts is thus shut up. Fontana also thinks it possible that the bile may be so attenuated and thin, that it may transpire through the liver into the blood, and thus bring on a jaundice.†

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[*] Frerichs, *Klinik d. Leberkrankheiten*, Braunschweig, 1858, Bd. i. p. 168.

[†] Portal, *loc. cit.*

[‡] Richard Mead, *Medical Works*. Edinburgh, 1763, vol. i. p. 34.

The cause of the jaundice after viper bites is exceedingly obscure. Galen does not, even in this age, find himself alone in believing the jaundice to be hæmatogenous. This view is in some slight degree borne out by the experiments of my friend and colleague Dr. Lauder Brunton. In the course of his laborious and invaluable investigations into the action of the Indian snake poisons, he found that under the influence of the viperine poison, the red blood corpuscles became altered in shape and were crenated. From this change in the corpuscles, some might adopt a theory of hæmatogenous jaundice as an explanation of the jaundice from the bites of vipers, just as Leyden has taken into service, for the explanation of the jaundice seen in phosphorus poisoning, the fact that phosphoric acid destroys the red corpuscles.

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* He doubtless means irritable in the sense of Haller, that is, that the nerves do not contract on the application of stimulus.

† Felix Fontana, *Traité sur le vénin de la vipere*, Florence, 1781, t. i. p. 67.

CHAPTER XXVIII.

ICTERUS GRAVIDARUM, EMBRYONUM, NEONATORUM, INFANTUM, MENSTRUALIS.

PREGNANT women sometimes suffer from jaundice, and this fact has been spoken of by nearly every writer on the diseases of pregnancy in modern times, although it cannot be said that much light has been thrown upon the nature of the disorder by these efforts. The interest in this variety of jaundice has been much increased, since its relation to *icterus gravis*, and acute yellow atrophy, has been noted.

Spaeth believes that the disease is very rare. Out of 33000 pregnant women, he only met with five cases of jaundice, three of which were simple, and two fatal.* During the autumn of 1876, when a good many cases of simple jaundice came to St. Bartholomew's Hospital, I met with two women, both in the 7th month of pregnancy, and both 35 years of age, who were jaundiced. No cause for the jaundice could be made out, and I was told that it disappeared a few days after delivery in each case.

Another woman, aged 34, in the sixth month of pregnancy, came to me in July, 1877, having been jaundiced two days. The urine contained bile pigment; and the skin was slightly, but certainly, yellow: the jaundice lasted only a fortnight, at the end of which time it was all but gone.

Dr. Fleetwood Churchill says that jaundice is more common amongst women of fair than dark complexion, and in winter than summer.† Most authors think that a plugging of these last; but it is not known if the process continue after delivery and during suckling. The continuance of the process during suckling would of course destroy the theory. The fatty infiltration of the liver certainly goes on, as the researches of Sinéty have shown.[*]

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* Spaeth, *Wien. med. Woch.* 1854, quoted in *Monatsschrift f. Geburtsk.* 1863, Bd. xxi. pp. 89 and 90.

† Fleetwood Churchill, *On the Diseases of Women*, Dublin, 1874, Sixth ed. p. 593.

Virchow suggests that in pregnant women the lower border of the liver may be turned round by the advancing uterus, a state which he says he has seen, but without causing jaundice. He also suggests that the liver and ducts of persons who have laced tightly, may be stretched by the rising uterus, and so a considerable jaundice may take place.[†]

Ficinus noted, in his own wife, the appearance of jaundice four times in four pregnancies, one after another. It would seem that the jaundice came on only in the last months of each gestation.[‡]

Of course those diseases which bring on jaundice out of pregnancy may cause it during pregnancy. The physician must not therefore at once pronounce the jaundice to be simple, but must make a careful physical examination, and only in default of other evidence make the diagnosis of simple jaundice.

It is well known that the skin of some women acquires a darker colour during pregnancy. This may possibly be mistaken by the heedless for jaundice, but the conjunctiva and urine would at once decide in the negative.

The treatment of the simple jaundice of pregnancy should not be active. The bowels must be regulated by mild laxatives, and small doses of the alkaline soda salts given by the mouth as well. The older writers specially note that emetics must not be employed on account of the danger of causing abortion, and this brings in the consideration of a jaundice in which abortion is very common. There can be no doubt that jaundice is often followed by early delivery, but it may be doubted if means exist to distinguish the early stages of this jaundice from the more simple kind. Hervieux says that the labour comes on from five to eight days after the first onset of the jaundice, but that in one of Bardinet's cases it was from six weeks to two months after.[*] The life of the fœtus is almost always lost,[†] but in this variety of jaundice that of the mother is spared. The fœtus is sometimes jaundiced like the mother, [See *Icterus Embryonum*] but this is not common.

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[*] L. de Sinéty, *de l'état du foie chez les femelles en lactation*, Paris, 1873.

[†] Virchow, *Gesam. Abhand.* Hamm, 1862, pp. 757 and 777.

[‡] Ficinus, *Monatsschrift f. Geburtskunde*, 1863, Bd. xxii. p. 146.

With the last, the grave form of *icterus gravidarum*, it would seem that Burns was in some degree acquainted.[‡] Ozanam noted the death of the mother and fœtus in a case of rapid jaundice,[§] and Frerichs' figures showed that one half of the cases of acute yellow atrophy were seen in pregnant women.[‖] After this, the relation of *icterus gravis* to the *icterus gravidarum* could no longer be doubted. It must also be remembered that in epidemic jaundice, the pregnant women nearly all suffer severe symptoms, such as coma, delirium, and the like, while the men and unimpregnated women show only the symptoms of simple jaundice. A certain proportion of the women attacked by epidemic jaundice die, while nearly all miscarry or abort with death of the fœtus. The phænomena of the disease do not appreciably differ from those of ordinary acute yellow atrophy. The diagnosis, treatment, and prognosis, are the same as in acute yellow atrophy.

The prognosis in all cases of *icterus gravidarum* must be grave enough if the proportion given by Spaeth hold in all cases. Out of his five cases, two ended fatally. It seems likely that this rates the danger too high; but the risk which the patient runs must always be kept in mind, as the tissues of a pregnant woman are only too well prepared to carry on the process of acute yellow atrophy to the fatal end.

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[*] Hervieux, *Gaz. méd. de Paris*, 1867, p. 290.

[†] See some cases by Monks, *Brit. Med. Journ.* 1876, Vol. ii. p. 278.

[‡] Burns, *Principles of Midwifery*, Lond. 1824, 6th ed. p. 231.

[§] Ozanam, *de la forme grave de l'ictère essentiel*, Thése de Paris, 1849, p. 50.

[‖] Frerichs, *Klinik d. Leberkrankheiten*, Braunschweig, 1858, Bd. ii. p. 243.

ICTERUS EMBRYONUM.

The fœtus of a jaundiced woman is sometimes jaundiced like the mother. Underwood, a good observer, and a man of great experience, says that this is exceedingly rare;[*] and Frerichs, that the jaundice must have lasted some weeks for the fœtus to take on a yellow colour; for in cases in which the jaundice appeared only 5 to 14 days before delivery, no changes in colour could be seen.[†] Sylvius says he has seen many children born jaundiced; he does not, however, distinguish between those yellow at birth, and a few days after.[‡] Kerckring was one of the first to find the fœtus of a jaundiced woman yellow. An eight months' child was born dead, and seemed as if made of wax, and scarcely like human offspring.[§] The infection of the child by the mother is often fatal to the life of the former, as abortion appears to take place very readily; and the child, even if born at full time, is often dead.[‖] And if the child be born alive, death may overtake it within the month.[*] The dissection of the gall ducts, in the two cases in which I can find that it has been done,[†] has shown them to be plugged with mucus, a very noteworthy appearance. The prognosis, however, is not absolutely fatal, for Vaillant has recorded a case in which the mother was jaundiced and the child was born jaundiced, yet it recovered when about a month old;[‡] and Budd gives a case in which the child was born as "yellow as a guinea," but acquired the natural colour in two or three days.[§]

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[*] Underwood, *A Treatise on Diseases of Children*, Lond. 1805, Fifth ed. Vol. i. p. 27. He says that women do not infect their children unless they suckle them, and that the infant must be weaned before it can be cured.

[†] Frerichs, *op. cit.* Bd. i. p. 113.

[‡] Sylvius, *Prax. med.* Lib. i. cap. xlvi. § ii. in *Op. Med.* Amstelod. 1579.

[§] Kerckring, *Spiceleg. Anat.* Amstelod. 1670, p. 118, Obs. lvii. The bones were likewise yellow. Kerckring seems fond of sensational descriptions of these fœtus: he says they have the shape of fiends, *monstrum informe*, and the like. This case has been copied far and wide as if of Bonetus' own observation (*Sepulchretum*, Lugd. 1700, t. ii. p. 333) but he has copied simply from Kerckring.

[‖] See Joseph Frank, *Prax. med. univ. præc.* Lips. 1843, pars iii. vol. ii. § i. p. 302. He gives the older bibliography, greater part of which I have been unable to see. Frerichs likewise gives a reference to Finke (*De morbis bilios. anomalis*) whose book I cannot find. Peter Frank records one case at Vienna. (*De curand. hom. morb.* Viennæ, 1821, Lib. vi. pars iii. p. 299.

Lobstein has described under the name kirrhonosis a disease of the embryo and fœtus, in which the serous and transparent membranes are tinged of a fine yellow gold colour.[||] This state does not, however, seem to have any relation to jaundice, although used by Braun in this sense.[¶]

Bile pigment, bile acids, and tyrosin, were found in the blood of a fœtus whose mother died, giving birth to it, from acute yellow atrophy. The abstract, which only I have been able to see, does not state if the fœtus were jaundiced.[**]

ICTERUS NEONATORUM.

The term *icterus neonatorum* is used in different senses by different writers. By some it is used to signify a mere physiological phænomenon, unworthy of the name of a disease; by others, though few in number, to mean a grave disorder, in which death may not unfrequently overtake the patient. In these pages I shall throw in my lot with the majority, and speak of those changes in the colour of the skin which follow birth as the *icterus neonatorum*. Seux has proposed to give the name of local jaundice to this state, leaving the name of general jaundice to the real disease hereafter to be described as *icterus infantum*.[*] Joseph Frank likewise divides the jaundice of the new-born into the false and the true.[†] Other names besides *icterus neonatorum* have been proposed; as the *color icterodes* of Juncker,[‡] the *aurigo neophytorum* of Sauvages,[§] or the erythrosis, erythiasis, or *icterus benignus* of other authors.

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[*] Baumes, *de l'ictère des nouveaux-nés*, 1806, 2e éd. p. 45.

[†] Wrisberg, *Descript. anat. embryon.* Götting. 1764, obs. i. and Baumes, just quoted.

[‡] Vaillant, *Diss. sur l'ictère des nouveau-nés*, Thèse de Paris, 1816, p. 21. See also Panarolus, *Iatrologismorum sive observationum med. Pentecostæ quinque*, Hanov. 1654, Lib. iv. obs. xliv. p. 136.

[§] Budd, *on Diseases of the Liver*, London, 1857, 3rd ed. p. 224.

[||] Lobstein, *Répert. gén. d'anat. et de phys. path.* 1826, t. i. p. 28.

[¶] Braun, *Allgem. Wien. med. Zeitung* 1863, Jahrgang viii. p. 281.

[**] Valenta, Virchow and Hirsch's *Jahresbericht f.* 1869, Bd. ii. p. 149.

The first monograph upon *icterus neonatorum* was, according to F. L. Meissner,[||] published in 1669, at Basle, by Dommelius. Deleboe Sylvius remarks that he has seen children come into the world yellow, and jaundice appear soon after birth.[¶] The first, however, to make any distinction between jaundice and the yellowness of infants was Juncker,[**] followed later on by John Storch.[††] Morgagni noticed the presence of jaundice in 15 of his own children, and thought it due to changes in the circulation of the liver soon after birth.[‡‡] Baumes first published in 1785 a treatise on the jaundice of the

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[*] Seux, *Recherches sur les maladies des enfants nouveau-nés*, Paris, 1855, p. 249.

[†] Joseph Frank, *Praxeos medicæ universæ præcepta*, Lips. 1843, Pars iii. Vol. ii. Sect. ii. Fasc. i. p. 306.

[‡] Juncker, *Consp. Med.* Halæ, 1734, ed. 3tia, p. 728.

[§] Sauvages, quoted by Joseph Frank, *op. cit.* p. 305.

[||] F. L. Meissner, *Grundlage der Literatur der Pädiatrik*, Leipzig, 1850, p. 68. The bibliography of the monographs appears to be given fully. See also his *Forschungen des neunzehnten Jahrhunderts im Gebiete der Geburtshülfe, Frauenzimmer- und Kinderkrankheiten*, Leipzig, 1826, Theil iii. p. 131, for a review of the opinions held concerning *icterus neonatorum*. Cf. Joseph Frank, *Prax. med. univ. præc.* Lips. 1843, Pars iii. Vol. ii. § ii. Fasc. i. p. 305.

[¶] Deleboe Sylvius, *Prax. med.* Amstelod. 1679, Lib. i. cap. xlvi. § 11.

[**] Juncker, *Conspect. Medicinæ*, Halæ, 1734, ed. 3tia, p. 728.

[††] John Storch, *Abh. von d. Kinderkhten.* Bd. i. pp. 379, 381 (according to Engelmann's catalogue published at Gotha in 1749-51). Quoted by Joseph Frank, *op. cit.* p. 306, note.

[‡‡] Morgagni, *De sedibus, etc.* Epist. xlviii, § 60.

Owing to the want of agreement among authors in the use of the term *icterus neonatorum*, much caution must be used in comparing their results. Elsässer, who thinks that the conjunctivæ and urine are coloured in this disorder, states that the difference between the two sexes and the complexion of children have very little influence in causing the disease. In his lying-in hospital he found that two-fifths became jaundiced, quite independently of atmospheric influences.* Dr. Charles West, who believes the conjunctivæ and urine remain uncoloured, states that exposure to cold, or a vitiated atmosphere may be the cause of the disease. In the Lying-in Hospital at Dublin, for example, the children are taken great care of; and jaundice is rare. In Paris nearly all the children in the Foundling Hospitals suffer from the disorder, the air being bad and the children exposed to cold.† All writers agree that the inmates of Foundling Hospitals are far more prone to jaundice than the children born at home. Weakly children and those born before the full time seem to be more commonly attacked than the strong and mature. Ritter von Rittershain thinks that all cases of *icterus neonatorum* are cases of pyæmia,‡ but these are cases which will be discussed by themselves.

It is well known that the child newly born is covered with a layer called the *vernix caseosa*. When this has been washed off, as usually happens soon after birth, the skin of the child is red from an erythema. The face is often of a deep red with a tinge of violet. Soon after, if the skin be pressed so as to empty the blood-vessels, the colour is not white, but there is a distinct trace of yellow. This yellowness increases, and the red colour decreases, until later on nothing but a yellow colour is seen.

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* Elsässer, Schmidt's *Jahrbb.* 1835, Bd. vii. p. 317.

† Charles West, *Lectures on the Diseases of Infancy and Childhood*, London, 1859, 4to ed. p. 566.

‡ Ritter von Rittershain, Virchow's and Hirsch's *Jahresb. f.* 1868, Bd. ii. p. 644.

Out of Kehrer's 474 jaundiced infants he found 5·3 *per cent.* only jaundiced on the first day; 62·9 *per cent.* on the second; 24·1 on the third; and a few only began on the fourth to the seventh.* Thus the jaundice may be looked for most commonly on the second day. The same observer found that in one third of the cases the jaundice was over in the first five days. In the greater number it was over by the 6th to the 10th day; sometimes in the second or even in the third or fourth week. He noted that in nearly all cases the jaundice did not appear first in the conjunctiva, but in the skin.

Kehrer divides the *icterus neonatorum* into three degrees: in the first, the skin for one or more days plainly shows a yellow appearance. This he thinks a true jaundice, even if the conjunctiva and urine be not coloured, for in cases of death, the serous exudations are found coloured yellow; in the second, the skin is coloured pale yellow, save the soles of the feet, the palms of the hands, the scrotum and the like red coloured places; in the third degree, the colour is that of yolk of egg, lemon, or even orange coloured. Now of 690 children, Kehrer found that 474, that is, 68·7 *per cent.* were jaundiced within the first eight days; 214, that is, 45·1 *per cent.* jaundiced in the first degree; 190, that is 40 *per cent.* in the second; and 70, that is 14·9 *per cent.* in the third degree. Kehrer concludes that two thirds of all children are more or less jaundiced during the first week. These observations it must be remembered were made in a lying-in hospital. Sex had scarcely any influence; nor was the jaundice seen much more commonly in twins, or first or later children. When labour comes on before the due time, jaundice is then oftener seen in the child, something like 17 *per cent.* more often. If there be an unnatural presentation, or long labour, there seems some evidence to show that jaundice is somewhat more common in the child. The time at which the meconium is evacuated seems to have no influence on the appearance of the jaundice.*

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* Kehrer, *Oesterr. Jahrb. f. Pädiatrik*, 1871, Bd. i. p. 85.

Porak made use of the time when he was resident assistant at the Cochin Hospital, in Paris, at which there are two or three deliveries daily, to make observations on the jaundice of the new-born, and especially on the time at which the umbilical chord should be tied. Like Kehrer, he divides the disease into three degrees of varying intensity. In the first, the colour is seen only over the face, chest, and back. It commonly begins in the face, sometimes, however, on the chest, where it is usually more marked than on the other places. In this first degree, the colour is very pale and lasts but a short time. The conjunctivæ are always white. This jaundice begins at the end of the first day and is over by the third or fourth. In the second degree the colour is more widely spread; the belly and the upper part of the fore and hind limbs are coloured; the feet and legs, hands and fore arms, are not usually coloured. The conjunctivæ are ordinarily yellow. This jaundice begins very rapidly, and lasts longer than in the first degree, from three to six days. It is almost always gone by the sixth or seventh day. In the third degree, the jaundice is general, and appears in the hands and feet. Porak observed 248 infants from the month of August 1877 to the end of the year. He found that 20·16 *per cent.* showed no jaundice; 13·71 *per cent.* showed the first degree; 36·69 *per cent.* the second; and 29·5 *per cent.* the third degree. He found nothing which he could distinctly set down as the cause of the jaundice.†

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* Kehrer, *Oesterreich. Jahrb. f. Pädiatrik*, Jahrg. 1871, Bd. i. p. 71.

† Porak, *Revue mensuelle de Méd.* 1878, p. 342.

to have their origin in a metamorphosis of the red blood corpuscles, and that they are signs of a hæmaphæic jaundice. But they admit that the masses are sometimes seen in a true jaundice from retention.

Besides the yellow masses, the presence of indifferent sediments is noted; such as crystals of urate of soda, hyaline, epithelial, or fatty, cylinders, blue masses of indigo, white globules, cells from the urinary passages, crystals of uric acid and of oxalate of lime.*

In the cases in which the skin of the child only is coloured, it would seem best to use Billard's hypothesis. Billard, it has been said, thought the jaundice due to changes in the circulation of the skin; the fading of the erythema, which comes on soon after birth, leaving behind it a yellow tinge, like a fading bruise. This view is supported by the fact that the yellowness is most marked where the redness has been greatest.

This explanation of the *icterus neonatorum* does not hold good if the conjunctivæ and urine be coloured. It must be admitted by all that there are some cases of true jaundice in the new-born. How then may these be explained? This will be fully discussed under the head of *icterus infantum*, to which the cases of true jaundice more properly belong.

The diagnosis depends upon the tint of the conjunctivæ and urine. If these be uncoloured while the skin of the new-born child is yellow, there can be little doubt that *icterus neonatorum* is present. It is important also to notice that the spot pressed by the finger is yellow. It is always well, however, to remember Dewees' advice, and in all cases of doubtful jaundice to examine the child most carefully, lest a true jaundice be present.†

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* Jules Parrot and Albert Robin, *Revue mensuelle de méd. et de chir.* 1879, t. iii. p. 374.

† Dewees, *Treatise on the Physical and Medical Treatment of Children*, London, 1826, p. 304.

The prognosis in the spurious jaundice may always be good. If real jaundice be present, it becomes of course somewhat more serious, though even then the result is commonly good.[*]

It is very rare for the jaundice to return; Porak has noted two such cases.[†] Kehrer says it sometimes happens. On the second to the fourth day, the skin becomes yellow, and after this has lasted one to three days, the jaundice disappears to return again on the fourth to the eighth days, and in about 24 hours again to disappear.[‡]

In the way of treatment little is needed. It may be advisable, to please the mother, to give a grain or two of rhubarb or magnesia; but no active treatment should be thought of. The process, being simply a physiological one, should not be interfered with.

ICTERUS INFANTUM.

New-born infants seem to be often seized with true jaundice,[§] the eyes being coloured yellow, and the urine staining linen. It differs very greatly in character, being sometimes a serious, sometimes a trifling, affection; lasting only a few days, or perhaps during the life of the child. This jaundice may be considered under several heads.

i. The jaundice of infants described by some authors seems to have the closest agreement with *icterus neonatorum*, save that the conjunctivæ and urine are coloured. It arises about the same time. The child seems to ail nothing. The stools have commonly a natural colour. The pulse retains its natural number of beats. There is nothing amiss with the child save that it is jaundiced. A few days after the jaundice has set in, Seux has noticed an ophthalmia with an abundant secretion of pus, the colour of which pus is a deep yellow, evidently stained with bile.[*] It was seen in 11 out of 64 cases, and ran as favourable a course as the jaundice itself.

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[*] Burns thinks the disorder always most serious. (*Principles of Midwifery*, Lond. 1824, 6th ed. p. 796.)

[†] Porak, *Revue mensuelle de méd.* 1878, p. 350.

[‡] Kehrer, *Oesterr. Jahrb. f. Paediatrik*, 1871, Bd. i. p. 87.

[§] Seux (*op. cit.* p. 269) found a true jaundice in 64 out of 408 children whom he attended during the first days of life.

The nature of this jaundice is very obscure. I must own that I incline myself to the explanation which Frerichs has given. This observer has pointed out, and his statements have been borne out by Heidenhain's direct experiments, that, when the pressure of the blood in the portal vein is decreased, the bile already secreted in the gall ducts begins to pass into the blood.[†] Now on ligature of the umbilical chord, the whole supply of the blood which passed into the portal vein from the umbilical vein is cut off, and the pressure in the portal vein will thus be diminished. In strong children, says Frerichs, the balance is soon re-established, but in weakly ones, in whom the respiration is slowly developed, and the fœtal passages long remain open, there arises more or less of real jaundice.[‡] Frerichs was not the first to suggest some such explanation of the jaundice of infants; for Morgagni thought it might be due to some disturbance of the circulation in the liver just after birth;[§] Autenrieth is said to have held much the same views.[‖]

Peter Frank thought the jaundice might be due to a prolonged retention of the meconium;[¶] and when the great amount of bile in the meconium, and the likelihood umbilical chord ought not to be too hastily done. An early ligature causes less blood to be contained in the infant's vessels than a late ligature. The corpuscles are rapidly destroyed after birth, and therefore an excess of them being destroyed will cause jaundice.* I hope I have not misrepresented this author's opinions, but these appear to me the views which he sets forth.

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[*] Seux, *op. cit.* p. 253.

[†] For a more full exposition of this theory, see p. 252 of this work.

[‡] Frerichs, *op. cit.* Bd. i. p. 199.

[§] Morgagni, *de sedibus et causis morb.* Ep. xlviii. § 60.

[‖] Autenrieth, *Obs. quaedam phys. path.* Tübing. 1799. quoted by Kehrer.

Portal, *Observations sur la nature et le traitement des maladies du foie*, Paris, 1813, p. 147.

[¶] J. P. Frank, *De cur. hom. morb.* Viennae, 1821, Lib. vi. Pars iii. p. 366.

As to treatment, nothing should be attempted. Underwood, indeed, thinks a vomit of ipecacuanha very important, more important than the four or five grains of rhubarb which he recommends: for he says that whenever the rhubarb only has been given, and the vomit omitted, the jaundice has persisted at the end of the month.† It is, however, more in accordance with experience gathered elsewhere, to let the disease take its natural course, and attempt no therapeutic measures beyond ordinary placeboes.

ii. Seux has drawn attention to a jaundice of infants, attended by all the symptoms of a catarrh of the intestines, diarrhœa, heat and tenderness of the belly, and quickening of the pulse. The diarrhœa appeared the same day as the jaundice in the greater number of the cases, and in a few cases two or three days before. Still more rarely did the diarrhœa set in after the jaundice.‡ This does not always run so favourable a course as the first named jaundice, for some of the children die. In those who recover, the diarrhœa first ceases, then the jaundice disappears. It is noteworthy, that vomiting, according to Seux, is a very rare phænomenon. Now in the jaundice which accompanies catarrh of the intestine in grown-up persons, vomiting is often a prominent symptom.

The treatment must be directed to the intestinal the navel, there are scarcely more than twenty cases on record. More, indeed, have been recorded of bleeding from the navel; but even this is a rare disease. Roger says that out of nine to ten thousand infants he had only seen it once;[*] and Stephen Smith, that in 12 years and 6654 births, no case occurred in the Lying-in Hospital at Dublin.[†]

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* Porak, *Revue mensuelle de Médecine*, 1878, p. 601.

† Underwood, *A treatise on the Diseases of Children*, London, 1805, Fifth ed. Vol. i. p. 26.

‡ Seux, *op. cit.* p. 253.

The jaundice is sometimes noticed at birth. In other cases it is noticed on the second or third day, or even later: in Dr. Wilks' case, it was not seen until the child was a fortnight old, although no meconium but only white motions were passed.[‡] In Lotze's case it was noticed within the third week.[||] In those cases in which hæmorrhage from the navel complicates the disorder, the jaundice seems to appear before the hæmorrhage in about one half of the cases. Grandidier has collected 220 cases of umbilical hæmorrhage; of these 84 were jaundiced, and out of these 84 the jaundice appeared in 44 before the bleeding began.[||] In nearly all the cases in which the state of the stools is mentioned, they have been colourless: in two they are stated to have been green or dark; in Lotze's case they were not completely colourless till the last weeks of life. The urine likewise is high coloured and stains the napkins yellow. At first, nothing amiss can be found with the liver. It is not enlarged or tender. But if the child live, the liver may attain a very great size, stretching down to the right iliac region on one side, and to the lumbar on the other. At the same time the spleen may become enlarged. There is no pain on handling the belly or hypochondria. Ascites may or may not be present.

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[*] Roger, *Union méd.* 1853, p. 139.

[†] Stephen Smith, *New York Journal of Medicine*, 1855, Vol. xv. p. 73.

[‡] Wilks, *Trans. of the Pathological Society of London*, 1862, Vol. xiii. p. 119.

[§] Lotze, *Berlin. klin. Wochenschrift*, 1876, p. 438.

[||] Grandidier, *Die freiwilligen Nabelblutungen der Neugeborenen*, Cassel, 1871, p. 62.

months* and the child died after vomiting coffee-ground matter. Dr. Nunneley has recorded a case in which the child, jaundiced from birth, lived six months and 21 days.† Lotze's case lived into the beginning of the eighth month, and died of a broncho-pneumonia.‡ This I believe to be the longest case on record. The other known cases have varied from a few days to five months.

In my own case, the child lived 5 months and a fortnight.§

Of the cases of jaundice with hæmorrhage from the navel there seem to be about two boys to every girl attacked: so that sex has considerable effect in predisposing to this disorder. Nearly the same holds good with respect to jaundice without hæmorrhage. Another interesting fact is the tendency these cases of jaundice have, with or without hæmorrhage, to attack children of the same family.

The children at the moment of birth seem to be lusty and strong. In a certain number of the cases, they are said to be feeble.

Of the health of the parents nothing is known. Syphilis has been thought by some to be the cause of the perihepatitis and of the obliteration of the gall ducts, as well as of the growth of the connective tissue in the liver. No other syphilitic changes besides these have been found in the bodies of the children when examined. In about 4 out of Grandidier's 220 cases of hæmorrhage from the navel, both parents or one are said to be syphilitic. The cases have likewise nothing to do with hæmophilia; for in hæmophilia, jaundice may be said never to be present, and bleeding from the navel very rarely. Those cases which recover from their bleeding

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* Campbell, *Northern Journal of Medicine*, 1844, Vol. i. p. 237.

† Nunneley, *Transactions of the Pathological Society of London*, 1872, vol. xxiii. p. 152.

‡ Lotze, *Berlin. klin. Wochenschrift*, 1876, p. 439.

§ See below, p. 641.

In those cases of jaundice without hæmorrhage, grave changes have usually been found in the liver and its ducts. Underwood's case is, however, an exception. The liver was found twice its natural size, but its substance was sound and healthy. The gall bladder was filled by a deep yellow bile, and its ducts were permeable.[*] The child in this case died on the ninth day of life, having become yellow on the third. In all the others, great changes in the liver and ducts are spoken of. The longer the child lives, the larger the liver seems to become. It is of a deep olive-green colour, with a granular surface, and of considerable consistence. On section, there are seen islets of whitish tissue, surrounding the vessels in the portal canals, which contrast strongly with the deep green of the proper liver substance. (See Chromolithograph No. iv.) Under the microscope, the section shows very distinctly dark green islets of liver cells imbedded in broad bands of connective tissue. The overgrowth of the connective tissue is chiefly in the capsule of Glisson. The state of the gall ducts varies. In some, gall bladder and gall ducts are altogether absent. In another, the gall bladder is present, but the ducts changed into strings of connective tissue; or the gall bladder may be present only in rudimentary form. In another case, the gall bladder and cystic duct, as far as the duodenum, may be present, but only a thin thread from the liver represent the hepatic duct. In another, the *ductus choledochus* only may be absent, or dilated into a blind cyst, from which no duct passes into the duodenum.

Sometimes there are traces of old peri-hepatitis, on the under surface of the liver, in adhesions to neighbouring parts.

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[*] Underwood, *op. cit.* p. 30. In Mr. John H. Morgan's case, the liver substance is reported to be healthy, although there was complete obliteration. (*Trans. of the Path. Society of London*, 1878, Vol. xxix. p. 139.) In Mr. Glaister's case the liver is reported to be "large and congested." (*loc. cit.*)

of the connective tissue in the liver. Ligature of the ducts in animals leads to a cirrhosis not less marked than ir children.[*] It is likely, then, that all obliteration of the ducts is followed by a cirrhosis, and therefore by a portal congestion. This may prove of some importance in the explanation of umbilical hæmorrhage. For, if any hindrance to the blood passing through the liver exist, it seems clear that the blood would seek some other means for leaving the belly; and what way offers less obstruction than the branch from the left portal vein to the *ductus venosus*, and thence to the umbilicus? Pressure is then brought to bear upon the vessels of the navel not yet perfectly healed, and bleeding from them takes place. The theory of portal congestion explains why it is common in cases of umbilical hæmorrhage to have likewise hæmorrhages into the various parts supplying the portal vein with blood. This explanation receives further support from the observations of F. Weber, who found, in certain cases of umbilical hæmorrhage joined to jaundice, that large tracks of the liver fed by the portal vein showed marks of inflammation, and a number of the branches of the portal vein were thus blocked, and unable to let blood through them.[†]

In cases of hæmorrhage from the navel, it is common to find the fœtal passages open, especially the umbilical vein and arteries. Grandidier says that in the seven cases in which the gall ducts were either absent or closed, the umbilical vessels were three times open, once the umbilical vein only, and in the remainder nothing is said of their state.[‡]

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[*] Wickham Legg, *St. Bartholomew's Hospital Reports*, 1873, Vol. ix. p. 161. At the end of the paper there is a comparison between the artificial cirrhosis and that caused by congenital deficiency of the ducts.

[†] F. Weber, *op. cit.* p. 12. Lhommeau (*Bull. de la Société anat.* 1842, année xvii. p. 52) found, besides other hæmorrhages, the interior of the gall bladder lined with blood.

[‡] Grandidier, *op. cit.* p. 69.

ployed. Dubois recommends the ligature *en masse.* The child being laid on its back, two hare-lip pins are passed through the skin at the root of the funis at right angles to each other, care being taken to avoid wounding the peritonæum. A ligature is then put around each needle in the form of a figure of eight, and lastly round the root of the navel itself.* Should I ever be so unfortunate as to be consulted in one of these cases, I should be disposed to use at first the perchloride of iron, aided by the compression of a leaden disc. This failing, the ligature *en masse* may be employed, as a last resort. Should any hæmorrhage from the navel be looked for, as in cases in which children born before in the family have suffered the like, it would seem best to be most careful in tying the funis, and likewise to avoid all rough treatment of it. After the chord have fallen, it would seem well to cover it with collodion. Treatment of the mother during pregnancy does not seem desirable.

Congenital deficiency of the common bile duct, the cystic and hepatic ducts ending in a blind sac; cirrhosis of the liver.

A POOR woman brought her baby, a litttle girl, to me, at St. Bartholomew's Hospital, on June 24th, 1875. The child was then seven weeks old. The mother said it was jaundiced at birth, and that the tint since birth was becoming deeper. The eyes at birth were yellow. The motions were said to be quite white, like curds and whey, and the water was said to be yellow. After birth the child is said to have had, for three weeks, a breaking out on the skin "more like small-pox with yellow heads." There was no bleeding from the navel after birth. This is the seventh child; none other has had jaundice or bleeding from the navel. The six children are alive and well. She has never had any miscarriages.

The child is now universally jaundiced, with small hæmorrhages like flea-bites all over the arms. The child snuffles, but has no rash now on skin, or sores about vagina or fundament. The child coughs, and all over the chest may be heard sibilant rhonchi. The liver is not to be felt. The amount of dulness seems natural.

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* Dubois, *Arch. gén. de Méd.* 1849, Vol. xxi. p. 192, note.

grammes, universally jaundiced, and wasted. No fat apparent anywhere.

Nothing unnatural in brain or membranes. Fontanelles widely open.

No fluid in peritonæum or pleuræ. The pericardium and heart natural.

The upper lobes of both lungs natural; the lower lobes are solid, plump, sinking in water, not depressed below surface of pleura, nor is pleura wrinkled. The cut surface is smooth and shining, and no fluid escapes on pressure.

The intestines contain colourless fluid, no solid fæces. They are natural in appearance.

The round ligament of liver is natural. The portal vein and hepatic artery appear quite natural, and free from clots. The gall bladder is shrunken, holds a small amount of a yellow fluid, and the cystic duct open without any winding into a cyst, the size of a largish marble, placed to the right side of the portal fissure between the liver and duodenum in the hepato-duodenal ligament. This cyst likewise receives the hepatic duct coming from the liver. It is a blind sac, and no passage can be found into the duodenum. The cyst is attached to the duodenum by a broad thin membrane, in which no duct can be found. The cyst is lined by a membrane about a millimeter thick, showing numerous small vessels, but otherwise closely resembling an hydatid cyst; it peels off with very little trouble from the outer wall of the cyst. It lines the whole of the cyst, except where the cystic and hepatic ducts enter, and here it is perforated by two round holes. The cyst holds a yellowish fluid. On attempting to dissect the hepatic duct, it is found free, and holding a yellowish fluid as far as a few lines from the liver. Here the walls of the duct become very thin and fibrous, the open mouths of a few narrow ducts being seen to open into it. On dissecting beyond this fibrous band into the right lobe, the duct from the right lobe is found to be greatly dilated, and to hold a quantity of thick bile; after being thus dilated for half an inch, however, it quickly becomes of small size, and cannot be followed with a fine pair of scissors. The duct from the left lobe cannot be followed at all.

The liver, stomach, pancreas, and duodenum weigh together 270 grammes. The liver is of a deep olive-green colour, the surface granular, and marked with numerous branching white lines. The largest of these white lines correspond to depressions. On section the cut surface is seen to be of the same colour as the peritoneal surface, but studded with islets of white tissue, which apparently days after birth, which accompanies the pyæmia of the new born, or umbilical phlebitis. This may likewise be attended by hæmorrhage from the navel. Dr. Herapath has recorded a good instance of this. A child was seized a few days after birth with jaundice, and erysipelas of the hand. There was a slight bleeding from the navel. After death, pus was found about the joints, and it is said also in the umbilical vein, and in the portal vein within the liver. The liver showed no abscesses. The gall bladder contained some colourless mucus, and the ducts were impervious.* Schuller has likewise recorded two cases of this sort. He calls them *icterus malignus*, or pyæmia, and the cause is formation of pus in the umbilical vein. The cases are as follows: two infants, weakly, and born at full time, came under observation at 8 and 10 days old: both the mothers were discharged well. The one child was bright yellow; the other dark. In the one the temperature was slightly raised, and in two days became very high, and the colour of skin became dark orange. With the fever, nervous symptoms appeared. The mucous membrane of the tongue dry, and blood followed attempts to cleanse it. The child sucked still, and had no vomiting. On the fifth day of the disease, convulsions of the cervical muscles, and ecchymoses were noticed. The yellow colour became bronze-like; sucking ceased, stools dark yellow; death next day, blood and pus escaping from the umbilical arteries. In the other case, the temperature was natural at first, but on the third day of observation fever appeared, with a tender belly, constipation, and vomiting. The urine, though intensely yellow, yet held no biliphæin. On the fifth day, there was a distinct enlargement of the spleen; and on the seventh day, a bulla filled with bright red blood appeared on the mons Veneris. On the tenth day the child died. The navel was not healed, and forward four cases.* His first case was that of a strong well-nourished woman of 30, who in July 1864, the day after her fourth, natural, delivery, was seized with jaundice, gastric symptoms, and diarrhœa with colourless stools. The jaundice lasted about nine days, and was followed by a bronchial catarrh, so that good health was not set up until three weeks after delivery. The child was weaned, but lived a little over a month. On Sept. 1. six weeks after delivery, menstruation again appeared, but ceased the same day. The next morning, jaundice, and colourless stools: the jaundice lasting three or four days. At the end of September, the same appearances were repeated, save that the stools were said not to be colourless; and again at the end of October. On Nov. 28. the menses appeared in greater abundance but without jaundice, and they lasted six days. On Dec. 24. there was scarcely any appearance of blood, but jaundice, which lasted three days, and was accompanied with rather severe pains in the right hypochondrium. Lastly, on Jan. 24. 1865, a jaundice appeared with the same pains in the neighbourhood of the liver, which showed a slight increase in size. The jaundice lasted about eight days, and there was no further appearance of it, pregnancy coming to an end on Sept. 21. The child was born at full time but died eighteen days old. The mother menstruated regularly for a year, and was then lost sight of.

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* Herapath, *Medical Times*, 1854, p. 286.

The second case was that of a married woman, who had enjoyed good health up to her fourteenth year, but then suffered from attacks of convulsions and loss of consciousness, which disappeared in about a year. She enjoyed good health until her 30th year, when ten days before her fourth delivery, (March, 1866), convulsions set in from mechanical congestion of the kidneys.

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* Senator, *Berlin. klin. Wochenschrift*, 1872, p. 615. *Ueber menstruelle Gelbsucht.*

The fourth case was a widow, 45 years old, never delivered, fat and hysterical, but with no serious symptoms. Up to a year ago menstruation had been regular and lasted from 4 to 6 days. From this time the catamenia appeared at longer intervals, and before the period the patient was often slightly feverish. On the 15th September, five weeks after menstruation, she fell ill with severe general pains, loss of appetite, and loaded tongue. The next day jaundice appeared. Urine dark, but without definite reaction with nitric acid. Stools of ordinary appearance. The jaundice lasted 1½ days, and as it disappeared, so menstruation came on. Four weeks after, the lady again felt chilly, with pains about her, and noticed a slight yellow appearance of the face. The jaundice increased, and in three days was unmistakeable. The next day, the hæmorrhage again appeared with hæmorrhoids. The other troubles soon after disappeared.

Senator remarks that jaundice in relation to the female sexual system has been noted in acute yellow atrophy, in which disease so large a number of cases are pregnant women. He thinks there can be no doubt of the connexion between menstruation and jaundice. The jaundice is clearly due to some hindrance to the flow of bile into the duodenum, as shown by the colourless state of the stools. Senator does not think the periodic jaundice due to gall stones, for none was found. He acknowledges the difficulty of explaining the relations of menstruation and jaundice. Menstruation is, however, sometimes replaced by hæmorrhages from other organs, from the lungs, stomach, nose, kidneys. Before the hæmorrhage there must have been hyperæmia; and the hyperæmia and swelling may exist without hæmorrhages taking place, so that a hyperæmia of the liver may come on, and cause a swelling of the gall ducts, and their retention of bile.

CHAPTER XXIX.

ON BILIOUS DISEASES.

As much confusion has arisen as to what may be understood by a bilious disorder, it may be well to begin by defining that disease to be bilious which is complicated by the following symptoms: a bitter taste in the mouth, a yellowness of the tongue, thirst, loss of appetite, nausea or vomiting, constipation or diarrhœa; a headache, more or less violent, which sometimes may even pass into delirium; a sense of weariness and aching of the limbs. There is no evidence that the disease is accompanied by any increase or decrease, or any change whatever, in the secretion of the bile; and it is only by accident that jaundice is seen; for though jaundice not uncommonly complicates a bilious disorder, yet it is an accidental, and by no means a necessary, part of the state.

It will be seen that the symptoms of an acute bilious disorder are identical with those now commonly attributed to acute gastro-duodenal catarrh; and a proof of the connexion of these symptoms with the pathological state of the stomach has, by a fortunate accident, been given by Dr. Beaumont in the case of Alexis St. Martin;* and still further worked out by Broussais in his elaboration of the doctrine of gastritis,† so that a bilious disease simply means a disease attended by a gastro-intestinal catarrh.

It may well be asked: Why is the disease called bilious, if there be no evidence of any change in the secretion of the liver? A satisfactory answer to this eases that afflict the human body. In Galen, all fevers are due to the bile, especially those that are most acute and ardent. Bile also causes wakefulness, delirium, and phrenzies, as well as the short madness, anger; it is the source of the sharpness and intelligence of the mind, while the other three humours cause other moral effects. It always causes acute diseases, and many inflammations, as erysipelas, herpes, inflammation of the fauces, black cancerous diseases, phagedæna, and elephantiasis. A green tongue distinguishes the predominance of the bile, as other colours are caused by the other three humours.*

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* Beaumont, *Experiments and Observations on the Gastric Juice*, Edinburgh, 1838, Combe's edition, p. 99.

† Broussais, *Leçons sur les phlegmasies gastriques*, Paris, 1823, p. 113.

The teachings of Galen remained undisputed dogmas throughout the middle ages; but the humoral pathology was fiercely attacked by Paracelsus in the sixteenth century, although it may be said that he only displaced the humours, to put in their stead mercury, sulphur, and salt. He held that bile never caused any diseases, not even jaundice, and that it was a mere excrement.† His follower, Van Helmont, taught that it was no excrement, but a necessary balsam of life, *viscus in forma liquoris*;‡ and how could disease arise from such a noble liquor?

It was worthy of Sydenham, that bilious diseases make but a small show in his works. He speaks, indeed, of a *colica biliosa*,§ but this would appear to me to be little else than a description of the symptoms

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sort of *Clavis Pathologiæ*; or, Pathology Unopened; though, to my mind, if this were so, all satisfaction would be taken away from the study and practice of medicine.

* I have not given references to prove all these assertions, as the reader will find then all in the index to Kühn's edition of Galen. The references to the bile fill nine columns of closely printed type of an octavo volume.

† Paracelsus, *Opera*, Genevæ, 1658, vol. i. p. 486, de icteritiis; and p. 78, Paramirum, lib. iii. de origine morb. ex tartaro, tract. iv.

‡ Van Helmont, *Scholarum humoristarum passiva deceptio atque ignorantia*, p. 72. It is bound up and paged with his *Febrium doctrina inaudita*, Amstelodami, 1648.

§ Sydenham, *Obs. med.* Sectio iv. cap. viii. Greenhill's ed. p. 194.

also which sometimes comes up into the mouth, burning the fauces, setting the teeth on edge, and very sour and bitter, was called acid bile by Stoll, and said to be very common in the summer and autumn.* Now if this *humor biliformis* abound in the blood, there is bilious plethora, called polycholia, which makes itself apparent by vomiting, purging, sweating, and bilious urines with yellow sediment; this state either gets well of itself, or by the aid of emetics, purges or diaphoretics. But if it be not removed by some means, it causes an infinite number of diseases by metastasis; the symptoms varying according to the function of the organ to which the metastasis takes place.†

If the *humor biliformis* be carried to the brain, then there appear delirium, phrenzy, apoplexy, and every kind of convulsions; if to the eyes, blindness, sudden cataract, ophthalmia, and opacities of the cornea; if to the fauces, angina; if to the chest, then cough, pleurisy, pneumonia, hæmoptysis; if to the belly, cholera, dysentery, colic, diarrhœa, piles, dysuria, floodings and abortions; if to the joints, rheumatism and gout; if to the skin, erysipelas, miliaria, herpes, and scabies, petechiæ, urticaria. The ardent fever or *causus* also comes about when the amount of *materies biliformis* is very great; and so instead of the ordinary *febris biliosa*, the *febris ardens* is caused.

It will be seen how slight a difference there is between the teachings of Galen and those of Stoll as to the diseases caused by the bile. The symptoms described by Stoll are in the main those set out at the beginning of this chapter. He dwells specially on the headache, which is rarely wanting in bilious disorders, and is often racking. Sometimes the face is very red with bright eyes; but the eyes are more commonly tinged with yellow; the tongue thickly coated with yellow; a bad taste in the mouth; want of appetite; nausea and vomiting, a desire for cold and acid drinks; abundant sweats; the stools very yellow, as if rhubarb had been taken, stinking; the urine yellow; and the blood drawn in blood-letting shows a *crusta phlogistica* yellow while the serum is green and bitter.

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* M. Stoll, *Ration. Medendi*, Pars i. Viennæ, 1794, p. 28.

† M. Stoll, *Aphor. de cognosc. et curand. febribus*, Vindob. 1786, p. 114.

The cause of bilious disorders is very commonly, according to Stoll, some trouble in the digestion; the eating of food abounding in fat or oil, or any thing which quickly decomposes, or becomes acid in the stomach; the abuse of wine; the want of fresh vegetables; living in an unwholesome place, as a hospital or prison; weather, unseasonable either from extreme heat or extreme cold; a chill while the body is heated; anger; sorrow; shame; eating too much; damage to the body; an excessive bleeding; the puerperal state.

Such were bilious diseases in the system of Stoll. But before the appearance of the *Ratio medendi*, Bianchi had begun to classify *Morbi a secretione Hepatis, aucta, diminuta, abolita, depravata.*[*] These diseases he does not indeed call bilious; but the symptoms attributed to each may be recognised when we come to speak later of the teachings of Copland. A want of bile leads to flatulence, loss of appetite, worms; if the secretion be suppressed, Bianchi does not seem to think of a jaundice following, but he says the whole animal machine is put out of order from the interruption of the first coction in the *primæ viæ*. There follow *delirium, letargia, suffocationes, etc.* Of a depraved secretion there are three kinds: the first, those states which are perceived by the sense of touch: the second, those states in which the bile is more watery: and the third, in which the bile is muddy, (*limosa*) or, as we should say to day, more concentrated. Of an increased secretion, the chief symptom was the cholera. This appears to be an exhaustive division; and it has been followed by all who have spoken of diseases caused by changes in the secretion of the liver.

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[*] J. B. Bianchi, *Historia Hepatica*, Pars ii. Cap. vi. Genevæ, 1725, t. i. p. 161.

In England, also, after the conquest of India, at the end of the last century, there arose a school which may almost be called the English School of bilious diseases. Acute diseases were no longer spoken of as bilious; rather this name was applied to some chronic disorder of digestion, or to diarrhœa, attended by some unwonted colour of the fæces. Cullen refused to admit bile as a cause of fever, either continued or intermittent; but allowed it as a cause of cholera or diarrhœa.* The views of Stoll were set aside:† and in Andree's *Considerations on Bilious Diseases* published in 1788, the word bilious disease is applied to Bianchi's diseases from disturbances in the secretion of the liver; and much the the same classification followed. "Bilious complaint" and "biliousness" are now the words met with to signify the chronic disorder. Andree divides them into four heads: i. Redundancy of bile, which is more often seen in hot countries than in England; for it was the old theory that more bile was secreted by the liver in warm seasons than in cold; a view which is the foundation of much of the theory and treatment adopted by practitioners in India, even at the present day. This redundancy of bile, in Andree's opinion, caused diarrhœa. It would also cause vomiting, as that which is seen on first rising out of bed in the morning, and which might last months, and even years, without toms which accompany these disorders of the bile, and how they may be distinguished from other diseases. The bilious diseases of Andree, we have seen, show the symptoms caused by a long course of dram drinking, for jaundice cannot be admitted amongst bilious diseases. Copland's description of disorders of the bile seems to be that which has made most mark within the last forty years;* and I think it may be taken as a fair presentation of the opinions of those who attribute symptoms to changes in the bile; and I shall therefore take his description as one which conveys the opinions of his school.

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* Cullen, *First Lines of the Practice of Physic*, §§ li.-lxxi. and mcccclxxx.

† Dr. Joseph Ayre opens his book on the bilious complaint with these words: "The term bilious is frequently applied in an indefinite manner to disorders of the stomach, in which the functions of the liver are undisturbed; whilst many important affections, in the strictest sense bilious, are known only by names which . . . . convey erroneous notions of their pathology." (*Practical Observations on Disorders of the Liver*, Lond. 1821, Sec. ed. p. 1.)

The symptoms of a decreased secretion of bile, according to Copland, may be summed up in two words: constipation with dyspepsia. The causes of this decreased secretion are very much akin to those of dyspepsia, and the symptoms described seem to me just the same. There is the same want of appetite, lowness of spirits, flatulence, foul tongue, bitter taste, and muddy complexion; with high-coloured urine becoming thick on cooling. But the appearance which would be the most important of all, is the pale appearance of the stools, for it was thought that the amount of bile secreted was shown by the colour of the stools, and that the pale appearance of the stools was a plain indication that less bile was secreted by the liver; and to this decreased secretion of bile were set down all the other symptoms which we now look upon as dyspeptic merely.

In the same way there was held to be an excessive secretion of bile when the patient had copious fluid evacuations, highly coloured with bile; such was called bilious diarrhœa or cholera. Or if the patient vomited bilious matters, this was a bilious vomiting from excess of bile. This excessive secretion of bile them also probably absorbed again into the blood, that the fæces offer no means whatever for estimating the amount of bile. Still less, therefore, can inspection help. I think myself that the statements made by the physiological chemists on this matter must be accepted; and, to tell the truth, very little knowledge exists as to the cause of the colour of the fæces, either in health, or in disease. It is indeed known that a few drugs, such as iron or bismuth, blacken the stools, and that complete obstruction to the common duct will cause them to become clay-coloured; but the other causes of the varying colours remain almost entirely unknown. The only proposition that can be safely upheld is, that bile is not the sole cause of all the changes of colour.

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* Copland, *A Dictionary of Practical Medicine*, London, 1844, Vol. ii. p. 723. Of the Functional Disorders of the Liver.

If then the simple inspection of the stools be an unsafe guide in judging of the amount of bile secreted, is there any other evidence, in the present state of knowledge, which would justify us in asserting that there is an increase or a decrease of bile in the states spoken of by Copland? It must at once be answered that there is none whatever, on either side of the question. There is no proof that the secretion of the bile is altered; neither is there any proof that the bile is unaltered. The propositions which are the foundation of the whole theory, that bile can cause a diarrhœa, and that its absence leads to costiveness, cannot be looked upon as proved; the evidence, whether from physiological experiments, or reasonings from disease, being contradictory. It is a trite remark that medical theories should accommodate themselves to what is known in physiology; but nowhere does there seem greater need for keeping this in mind than in dealing with the diseases that are called bilious. The bile may, for ought known, undergo deep changes in the diseases called bilious, and the older physicians may have shown their accustomed penetration in the matter; but until before Sydendam, makes his *malade imaginaire* ask: Ai-je bien fait de la bile?[*] G. E. Stahl gave his sanction to, even if he were not the author of, the thesis with the extravagant title which explains that the vena porta is the port of all evils.[†] I suppose, too, that Kämpf's theory of infarctus marks the lowest point reached in medical speculation in the last century. And in our own time we have seen several physicians, of good repute, set forth and support theories about the liver and the bile, which unfortunately fall to pieces as soon as they are examined.

I would venture to propose that the use of the name "bilious," as applied to diseases or disorders, be discontinued. In the first place, it has been seen that the wildest confusion prevails as to the meaning of the word. No one's definition agrees with his fellow's. Modern German writers speak of diseases complicated with jaundice as "bilious." It is true that an acute disease complicated by jaundice is very commonly bilious in the sense of Stoll, because the jaundice is so often caused by an extension of the gastro-intestinal catarrh to the gall-ducts. But the bilious diseases of Stoll are so forgotten that I have known a German writer, making statistics, count cases of the bilious pneumonia of Stoll as meaning those complicated with jaundice. Here in England a bilious attack means vomiting with headache, as well as for a dyspepsia, which it is hard to persuade those who use the word to define. But Dr. Bence Jones has given a fresh meaning even here; and "biliousness" is, according to him, "only the faintest jaundice."[‡]

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[*] Molière, *Le Malade imaginaire*, Acte i. Scène ii.

[†] Gaetke, *Diss. de Vena portae porta malorum hypochondriaco-splenico-suffocativo-hysterico-colico-hæmorrhoidariorum*, Halæ, not dated, published in Haller's *Disp. Anat. Select.* Gotting, 1748, Vol. iii. p. 131. The name of Stahl in this edition runs at the top of the page as the author, thus: "Stahl de vena portae," etc.

[‡] Bence Jones, *St. George's Hospital Reports*, 1866, Vol. i. p. 194.

CHAPTER XXX.

BIBLIOGRAPHY OF ICTERUS EPIDEMIUS, ACUTE YELLOW ATROPHY OF THE LIVER, AND CONGENITAL CONSTRICTION OF THE GALL DUCTS.

IN this chapter I have put together the references to these three matters which I have met with in my reading. They do not pretend to be exhaustive; but it is possible that they may be of some use to students coming after me, who, like myself, may be interested in these states.

All the references which are marked with an asterisk are those which I have not myself verified.

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